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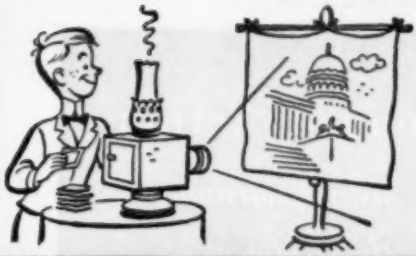

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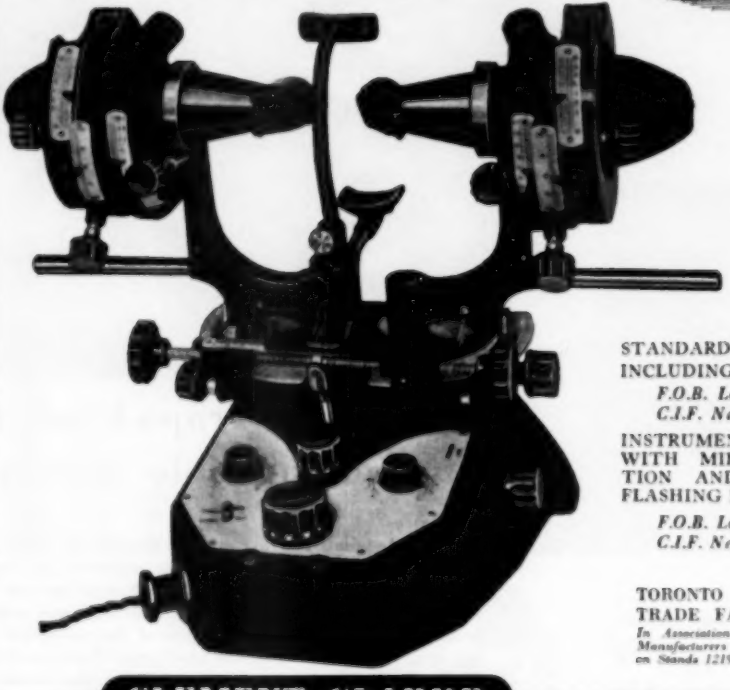

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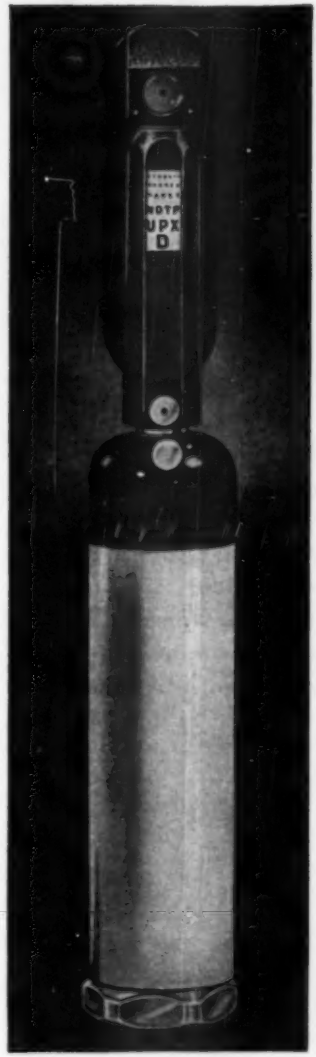

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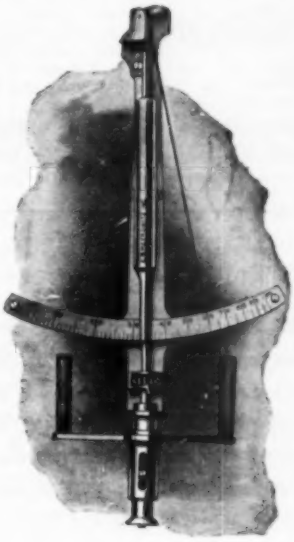

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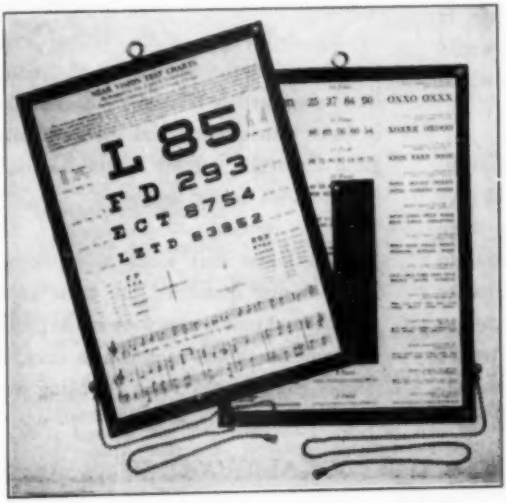

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ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education, and history 818

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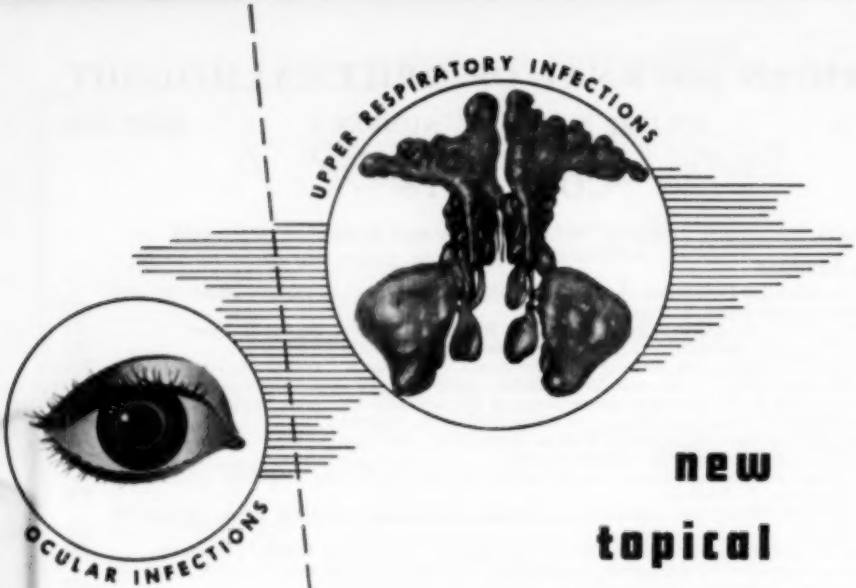

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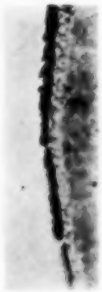
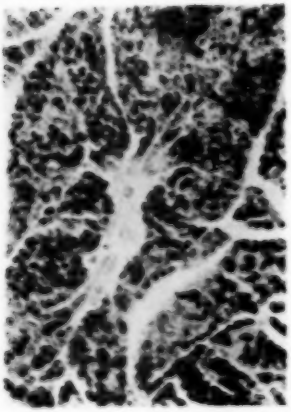


B. RAT EYELID



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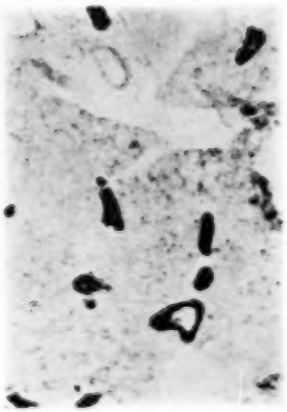

D. RAT SUBLINGUAL GLAND

FIG. 1 (BECKER AND FRIEDENWALD). HISTOCHEMICAL LOCALIZATION OF GLUCURONIDASE IN OCULAR TISSUES AND SALIVARY GLANDS

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 33 MAY, 1950 NUMBER 5

THE HISTOCHEMICAL LOCALIZATION OF GLUCURONIDASE IN OCULAR TISSUES AND SALIVARY GLANDS*

BERNARD BECKER, M.D., AND JONAS S. FRIEDENWALD, M.D.
Baltimore, Maryland

Methods for the localization in tissue sections of the enzyme catalyzing the hydrolysis of the glucuronide linkage were recently described.[1] The localization observed in such tissues as cartilage, bronchial mucous membrane, and Brunner's glands of the duodenum suggested a relationship between this enzyme and mucoid metabolism. It therefore appeared desirable to investigate various ocular tissues and the salivary glands.

In the method used in this work, glucuronidase activity is localized in the freshly frozen tissue section by its ability to hydrolyze 8-hydroxyquinoline glucuronide. The liberated 8-hydroxyquinoline is precipitated at the presumptive site of enzyme activity by ferric ions. This ferric hydroxyquinoline precipitate is then converted to Prussian blue. Glucuronidase activity is therefore represented by a blue precipitate.

In the eye, glucuronidase is localized in the ciliary body, conjunctival mucous membrane, cornea and in the coats of the larger iris vessels. The rabbit ciliary body (fig. 1-A) shows intense activity in the epithelium especially the superficial layer at the tips of the ciliary processes. This activity may be estimated quantitatively by the method of Fishman[2] and others, and compared with values for other rabbit organs. In Table 1 representative values for rabbit kidney, lung, liver, ciliary body, lacrimal gland, and harderian gland are indicated. It is apparent that the ciliary body has considerable activity per gram weight, even more than is found in the kidney or lung. Since this activity is mostly confined to the epithelium of the ciliary processes, the values for this epithelium must be very high.

The glucuronidase activity in the eyelid of the rat is for the most part intensely localized in the conjunctival mucous membrane (fig. 1-B).

In order to demonstrate activity in the rat cornea, it is necessary to incubate in the presence of a testes extract. The action of this testes preparation is not clear as yet, but it most probably acts by removing an inhibitor present in the cornea (for example, hyaluronosulfate). The corneal glucuronidase is primarily in the epithelium but is also found in stromal and endothelial cells.

The rat submaxillary gland, a so-called "mucous" type of gland, shows much activity throughout the acini of the gland with little or no activity in the ducts or vessels (fig. 1-C).

TABLE 1

GLUCURONIDASE CONTENT OF RABBIT ORGANS
(Expressed as gamma phenolphthalein liberated per gram tissue per hour at 38°C. from phenolphthalein glucuronide at pH 4.5)

Organ	Gamma per Gram per Hour
Kidney	160
Lung	247
Liver	6,630
Ciliary Body	360
Lacrimal Gland	150
Harderian Gland	125

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital. This study was supported by the Chalfant fund.

The sublingual gland is a "serous" type gland, and its glucuronidase activity is limited to the epithelium of the ducts with very little activity in the acini of the gland (fig. 1-D). This is in good agreement with the fact that the serous secretion has a mucoid element presumably added to it as it passes through the ducts of the gland.

The lacrimal and harderian glands show activity similar to that of the submaxillary gland.

Summary

1. In the eye, glucuronidase is localized in the epithelium of the ciliary body, the conjunctival mucous membrane, and in the cells of the cornea.

2. The "mucous" submaxillary gland has intense activity throughout the cells but the "serous" sublingual gland's activity is confined to the epithelium of the ducts.

3. The harderian and lacrimal glands show a glucuronidase distribution similar to that of the submaxillary gland.

4. The high activity found in the ciliary epithelium suggests that this tissue may be the site of synthesis of the vitreous mucoid.

1212 Eutaw Place (17).

References

1. Friedenwald, J. S., and Becker, B.: The histochemical localization of glucuronidase. J. Cell. & Comp. Physiol., 31:303-310, 1948.
2. Tallalay, P., Fishman, W. H., and Huggins, C.: Chromogenic substances: II. Phenolphthalein glucuronic acid as substrate for the assay of glucuronidase activity. J. Biol. Chem., 166:757, 1946.

DYSTROPHIES OF THE CORNEA*

The fifth Sanford R. Gifford Lecture

Everett L. Goar, M.D.
Houston, Texas

First I should like to express my appreciation for the honor of being invited to give the fifth Sanford R. Gifford Memorial Lecture. I am glad to contribute whatever I can to the memory of your beloved and distinguished member who was taken at the very peak of his career.

I have selected the subject "Dystrophies of the cornea," because of my interest in them for many years. It seemed better to attempt to cover the whole subject in what may seem to you a sketchy sort of way rather than to concentrate on one type because, while the literature is replete with articles dealing with the various types, it is exceedingly difficult to obtain a composite picture of the dystrophies. I was somewhat dismayed to find that so many Chicago ophthalmologists have written concerning the dystrophies, for it is like carrying coals to Newcastle for me to bring home some of the work that has been done here in your city.

The term dystrophy is somewhat loosely used and is often regarded as synonymous with degeneration. In fact it is so listed in the *Index Catalogue of the Surgeon General's Office*. To me there is a slight difference in that a dystrophy must be an anaplasia due to a nutritional disturbance, while degeneration may occur from other causes. It must be admitted, however, that most dystrophies are degenerations in that a process that starts as a mild nutritional disturbance usually progresses through stages of tissue degeneration, so perhaps it is not worth while to quibble about terms.

* From the Department of Ophthalmology, College of Medicine, Baylor University. Presented before the Chicago Ophthalmological Society, January, 1949.

When one delves into the subject of corneal dystrophies, he is struck first by the appalling number of articles written on the subject and next by the confusion in classification. Each type has from 3 to 6 names and usually an eponym is attached to it. It will be necessary in this discussion to use more than one name in order to identify the disease, but after that perhaps I can stick to one in order to avoid complicating the situation further.

The following seems to me to be a satisfactory classification of the dystrophies:

1. Fatty or lipoid degeneration
2. Marginal dystrophy
3. Band-shaped or zonular
4. Nodular dystrophy of Salzmann
5. Familial and hereditary
   - A. Granular
   - B. Macular
   - C. Reticular

   } Bücklers's classification
6. Endothelial and epithelial dystrophy

An occasional case is found which fits none of these types. It has to be regarded as unclassified.

There are also conditions such as arcus senilis and presenilis, cornea farinata of the aged, hyaline and amyloid degeneration, and Vogt's crystalline dystrophy that scarcely deserve discussion in a paper of this scope. Many of the conditions I shall speak of I have encountered myself; others I have had to borrow from the wider experience of friends. Only an ophthalmologist connected with a large clinic over a long period has the good fortune to see each type of dystrophy described in the literature.

Fatty or lipoid degeneration

This is encountered fairly frequently in adults and occasionally in children in chondrodystrophic dwarfs. Fatty degeneration secondary to trauma occurs frequently, but here we are concerned only with the primary forms. It is just as well to say at the outset that, although this condition is due to some disturbance in fat metabolism, the pathogenesis is unknown. Fats[1] occur in the body as neutral fats, phospholipids, and steroids. The part neutral fats play in metabolism is not well understood. The lipoids, however, exist in the tissue cells and in the blood serum and play an important part in tissue activity. Normally, however, they are quickly oxidized by an enzyme. It probably is the failure of oxidation to take place that allows fat to accumulate in and between the cells in abnormal amounts.

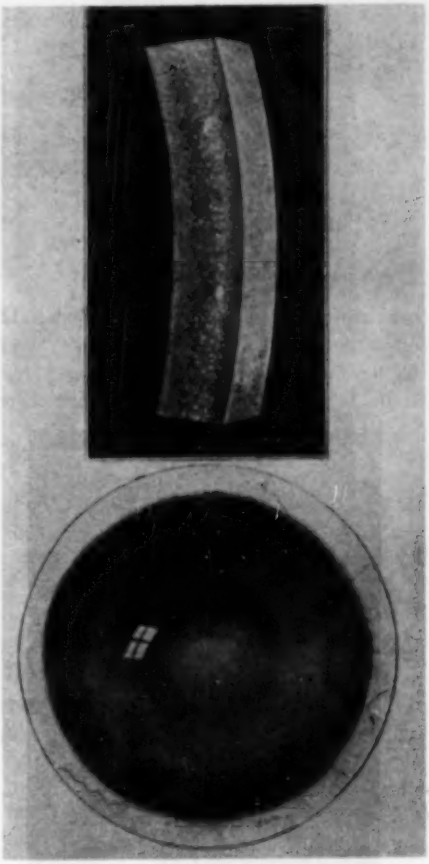

Fig. 1 (Goar). Lipoid dystrophy. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye*, published by Paul B. Hoeber, Inc.)

Not only may the lipoids so concentrate, but this induces deposition of the coarser neutral fats, and so in some of these cor-

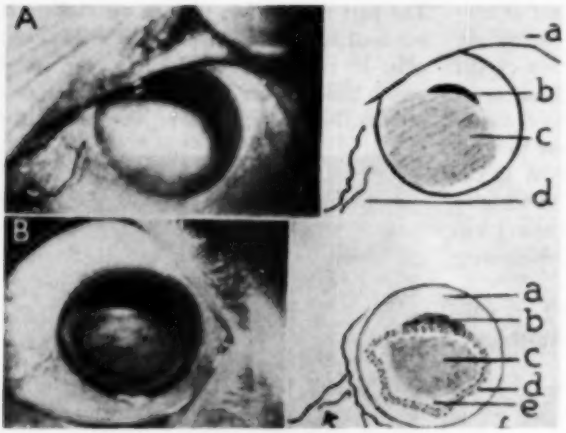

Fig. 2 (Goar). LIPIN KERATITIS. (Parker Heath's case. Reprinted with permission. From the *Archives of Ophthalmology*, volume 13, 1935.)

neas differential stains, such as Sudan III or osmic acid, will show fat deposits while others fail to do so. The latter type may contain cholesterol crystals or histiocytes filled with granules that may be lipoidal in nature.

Fig. 3 (Goar). HURLER'S SYNDROME. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

When fat metabolism goes awry, it may lead to peculiar pathologic entities, depending to some extent on the type of fat, the organ affected, and the reaction of the tissues. The abnormal fat deposit soon sets up a foreign-body reaction, and the reticuloendothelial cells, known variously as histiocytes or macrophages, appear to phagocytose the fat and so become foam cells.

As so often happens, Nature, when left to itself, overdoes the thing: the circulation is interfered with, transudation and exudation occur, and fibrosis ensues. This has been particularly well described by Parker Heath[2,3] who has made an exhaustive study of the subject. Heath objects to this being called a dystrophy and insists that it is a lipin interstitial keratitis.

Clinically the first sign of lipoid deposition of the cornea is a deep cloudiness which may begin either in the center or periphery and, if studied early with the biomicroscope, this is resolved into tiny dots or spherules which are droplets of fat infiltrating the stroma (fig. 1). Vessels from the deep limbal loops penetrate the substantia propria so that considerable vascularization occurs, though less than in the parenchymatous keratitis of hereditary syphilis. Thickening

of the stroma occurs during the active stage, especially in the posterior two thirds. These corneas are always left with considerable scarring, but vision may improve in young adults as in Heath's patient (fig. 2).

In 1919, Gertrud Hurler described two children, dwarfs, who had enlarged liver and spleen and corneal opacities. This added a new type to the four existing lipoidal dyscrasias—namely, Tay-Sach's disease, Hand-Schüller-Christian, Niemann-Pick and Gaucher's syndromes.

This condition, as in the case of most of the dystrophies, has several names—lipin keratitis of Hurler's syndrome, lipochondrodystrophy, dysostosis multiplex, and gargoylism.

When Berliner[5] reported (fig. 3) his three cases in 1939, only 20 cases had been recorded previously and 19 of these had bi-

Fig. 4 (Goar). HURLER'S SYNDROME. (Hogan and Cordes's case. Reprinted with permission. From the *Archives of Ophthalmology*, volume 32, 1944.)

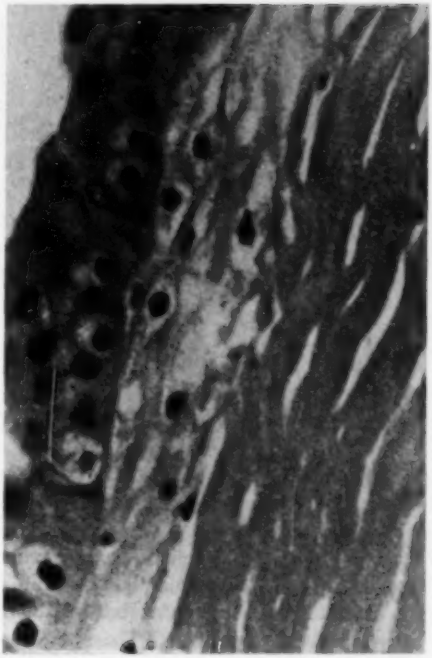

Fig. 5 (Goar). MICROSCOPIC SECTION, showing replacement of Bowman's membrane by macrophages. (Hogan and Cordes's case. Reprinted with permission. From the *Archives of Ophthalmology*, volume 32, 1944.)

lateral cloudiness of the corneas. Several cases have been reported since, notably three by Hogan and Cordes (fig. 4).[6] These children have an enlarged and often scaphocephalic head, protuberant abdomen, saddle nose, broad thick hands—in fact they look like gargoyles.

The clouding of the corneas begins near the end of the first year. The cloudiness increases gradually until the 4th or 5th year, after which it becomes stationary. Vascularization does not occur in these corneas as it does in adults. Sections show thinning and rupture of Bowman's membrane with infiltration of the membrane by large cells containing granular material (fig. 5).

The fixed corpuscles of the cornea are swollen and contain the same granular ma-

Fig. 6 (Goar). WHITE RING OF THE CORNEA. (Reprinted with permission from Duke-Elder, *Textbook of Ophthalmology*, volume 2, published by Henry Kimpton.)

terial as the histiocytes that have invaded Bowman's membrane. These granules do not take the stains for fat but, according to Hogan and Cordes, the granules are found much more abundantly in frozen sections than in those imbedded in paraffin and pyroxilin. They suspected, therefore, that the granules were lipin that had dissolved in the process of fixation. These children often die at an early age of intercurrent disease.

White ring of the cornea (fig. 6), first described by Coats in 1912,[7] is seen occasionally by those who use the biomicroscope routinely. It consists of an irregular, often broken, circle of white dots in Bowman's membrane. It is usually unilateral, and I have never found more than one ring in a cornea. It causes no irritation and the patient is not conscious of it. The granules are lipoidal and it has been suggested that they form as the result of a foreign-body irritation, although this is unproven. Personally I do not believe the cornea reacts in this manner to a foreign body, for the macula that remains after removal of a deeply imbedded foreign body, or after the small ulcer from infection has healed, does not form such a ring.

MARGINAL DYSTROPHY

This is a rather rare disease, and I have seen only one patient with the corneas severely involved. This (fig. 7) is a woman whom I first saw 10 years ago when she was 37 years of age. She had suffered from attacks of discomfort with her eyes for several years during which first one eye, then the other became congested and irritable. These flare-ups were prone to occur at the menstrual period. She was a thin, nervous woman and was allergic to many foods and external agents.

Her refraction was: R.E., +0.5D. sph. ⌒ −3.0D. cyl. ax. 105° = 20/20 − 2; L.E., + 0.25D. sph. ⌒ −0.5D. cyl. ax. 10° = 20/20. She had a recurrent pterygium nasally on the right cornea.

Inside the limbus and encircling the entire

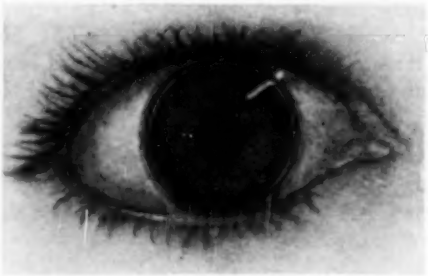

Fig. 7 (Goar). MARGINAL DYSTROPHY, furrow stage. By focal illumination. (Goar's case.)

periphery of both corneas was an infiltrate resembling arcus senilis, except that there was no clear space between it and the corneoscleral margin. The whole area was thinner than the cornea central to it, so a sulcus or gutter was formed in which vessels had slipped over from the limbal loops to penetrate the floor and walls of the furrow. The wall of the furrow next to the limbus sloped gradually, but the inner wall was more abrupt. The thinnest areas were above, and that in the right eye was thinner than in the left, being about one half the thickness of the normal cornea. The epithelium was intact throughout the furrow.

Nothing was found on physical examination to account for the condition except that her blood cholesterol and fatty acids were moderately increased.

She has had many changes of glasses, and in August, 1947, her refraction was: R.E., −4.5D sph. ⌒ +7.0D. cyl. ax. 32° = 20/20 − 2; L.E., −2.0D sph. ⌒ +5.0D. cyl. ax. 110° = 20/30 − 2. With an addition for presbyopia, she read fine print readily. There has been a steady increase in myopia and astigmatism during the years I have observed her, but ectasia has not yet appeared.

Marginal dystrophy, like all dystrophies, has been given several names, among them ectatic marginal dystrophy, peripheral furrow keratitis, and senile marginal atrophy.

Dr. Martha R. Folk[8] of Chicago, in reporting a case in 1943, stated that according to Gifford about 595 cases had been recorded. There must have been an error in printing, however, as Gifford's article states "Descriptions of 52 cases were found in the literature, the present 47 cases making a total of 559." Duke-Elder[9] says that about 100 cases had been described in the literature, of which 75 percent were in males. Dr. Folk's article gives an excellent bibliography, so it is not worth-while in this discussion to furnish further references.

This disease progresses very slowly so that it may never reach the stage of ectasia (fig. 8) and, although the cornea becomes quite thin, it may not rupture unless accident occurs. However, astigmatism which is due to flattening of the cornea in the region of greatest involvement becomes of a high degree, and vision may be considerably lowered.

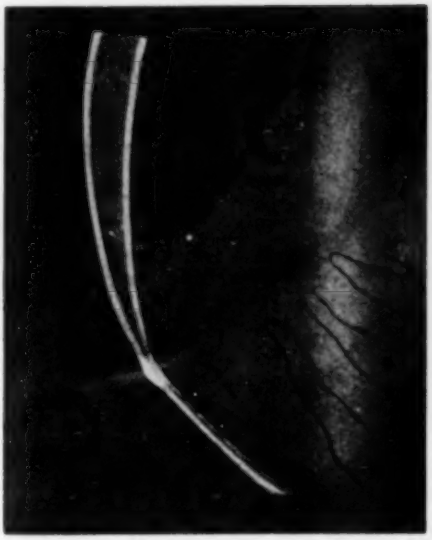

Fig. 8 (Goar). MARGINAL DYSTROPHY, ectatic stage. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

Histologic sections have been made (fig. 9) in the various stages of marginal dystrophy. Early, Bowman's membrane splits into fibrillas, and fat droplets may be found between them. The stroma is replaced by rather loose connective tissue, and the lamel-

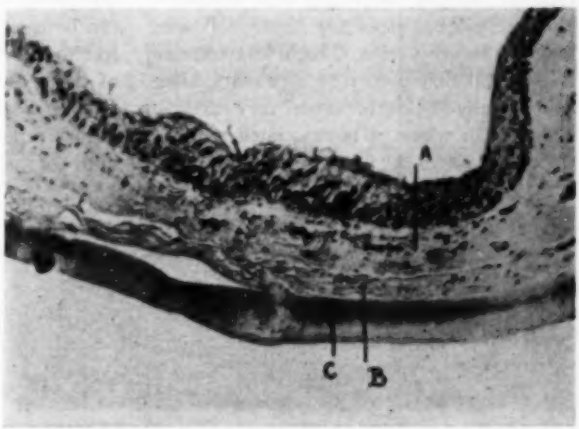

Fig. 9 (Goar). MARGINAL ECTASIA OF CORNEA. (A) Subepithelial tissue. (B) Remains of corneal lamellae. (C) Descemet's membrane. (Reprinted with permission from Duke-Elder, *Textbook of Ophthalmology*, volume 2.)

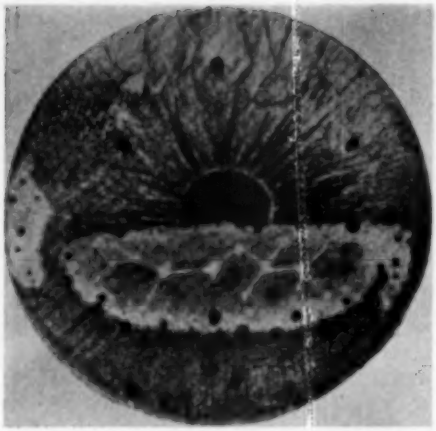

Fig. 10 (Goar). ZONULAR OPACITY. (Reprinted with permission from Duke-Elder, *Textbook of Ophthalmology*, volume 2.)

las become thin and disappear. Descemet's membrane remains intact, and, when the cornea becomes thin enough, it bulges through the furrow with the little remaining stroma. The epithelium does not disappear but becomes edematous and disorganized. Rupture usually occurs after the ectatic stage which may be delayed many years from the onset.

BAND-SHAPED OR ZONULAR DYSTROPHY (fig. 10)

All ophthalmologists are familiar with the type of zonular dystrophy that occurs in atrophic globes, especially those following long-continued uveitis. Much less common is the kind that occurs as a primary affection, usually in elderly people, very rarely in children, in whom it is associated with arthritis.

The older writers regarded the primary lesion as a deposition of lime salts. With the advent of the slitlamp, it was found that the first thing that happened was a turbidity in Bowman's membrane due to a fine granular deposit, probably calcium phosphates and carbonates, together with silicon and sulphur. Hyalinization of Bowman's membrane begins and dark holes appear in the membrane, probably where the corneal nerve fibers emerge. Bowman's membrane is gradually replaced by fibrous tissue and hyaline, and the deposition of calcium usually invades the superficial layers of the stroma.

Figure 11, taken from Fuchs's textbook, shows the characteristic calcification of Bowman's membrane and the fibrosis that has taken place between it and the overlying epithelium. The fibrous tissue has pushed its way through the brittle Bowman's membrane and is invading the underlying stroma.

Clinically zonular opacity usually begins in the superficial layers of the cornea adjacent to the limbus, occasionally in the central area. It always is found in the interpalpebral fissure. As soon as the opacity becomes visible, the small dark holes that are pathognomonic of the disease may be seen with the biomicroscope. The opacity increases in density, moving slowly across the cornea until the bands join in the central area. By this time the lime incrustation has become so thick that spots may flake off or can be easily removed. These eyes are subject to attacks of irritation and, in presence of the secondary form, often must be enucleated. Superficial keratectomy gives temporary relief in primary dystrophy and may improve vision considerably.

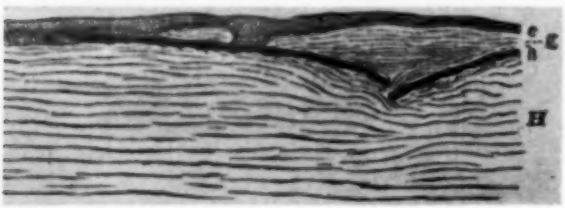

Fig. 11 (Goar). ZONULAR OPACITY. (e) Epithelium. (g) Connective tissue. (h) Bowman's membrane. (H) Stroma. (From Fuchs's *Textbook of Ophthalmology*.)

Fig. 12 (Goar). TYPE 1 WHITE LIMBUS GIRDLE. (From Vogt's *Atlas of Biomicroscopy.*)

WHITE LIMBUS GIRDLE

White limbus girdle, described and named by Vogt, resembles zonular dystrophy to some extent, although it does not involve the central area of the cornea. Vogt described two types, both of which start at or near the limbus in the interpalpebral zone. Type 1 has a clear ring (fig. 12) between the opaque area and the limbus as in gerontoxon, and shows dark holes similar to those in zonular opacity. Type 2 shows no such clear zone (fig. 13) and is often continuous with a raised opacity on the adjacent conjunctiva. This girdle may extend above and below the interpalpebral fissure, but never encircles the cornea as arcus senilis does.

The opacity is superficial, doubtless in Bowman's membrane, and the yellowish color seen when the conjunctiva is involved makes one think it is either lipoidal or hyaline degeneration. So far as I know histologic studies have not been made.

If looked for properly with the biomicroscope, this girdle is very common in middle-aged and older persons, especially in women. I have seldom seen it in persons under the age of 40 years but have found it in six percent of men above that age and in 30 percent of women.

The jagged edge of the central part of the girdle suggests a degeneration caused by sclerosis of the limbal vessels. The best way to demonstrate the girdle is by retro-illumination from the iris near the chamber angle, or by sclerotic scatter.

SALZMANN'S NODULAR DYSTROPHY (figs. 14, 15, 16, and 17)

This disease was described by Salzmann[10] in 1925, and it differs from all other dystrophies in that it always follows phlyctenular keratitis which is, of course, inflammatory, but the nodules themselves are degenerative in nature and show no signs of inflammation. Moreover, the descriptions of the few pathologic specimens that have been

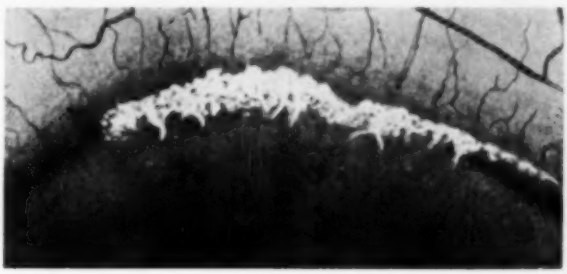

Fig. 13 (Goar). TYPE 2 WHITE LIMBUS GIRDLE. (From Vogt's *Atlas of Biomicroscopy.*)

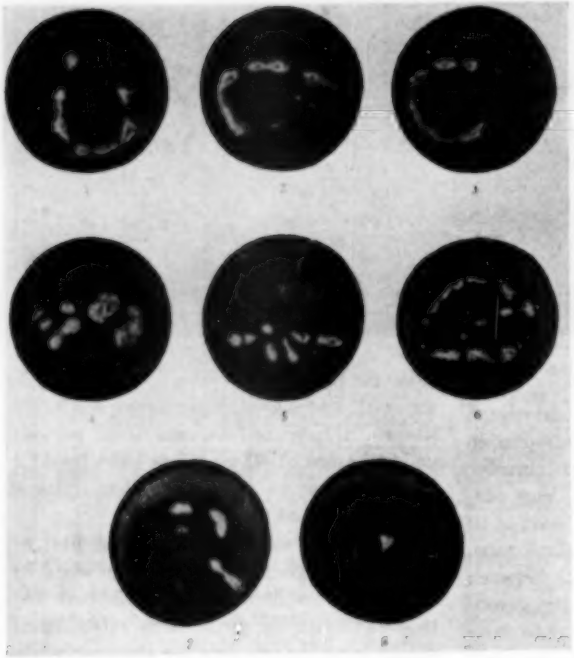

Fig. 14 (Goar). SALZMANN'S NODULAR DYSTROPHY. The top three pictures are of a young adult, taken at three-month intervals. Other pictures are of different patients, showing various conformations and distributions of nodules. Pictures 4, 5, and 6 display intense vascularization. (Reprinted with permission from Brown and Katz: *Archives of Ophthalmology*, volume 13, 1935.)

examined differ so widely that it might be thought the pathologists were speaking of different diseases. Salzmann described 23 cases which he saw in his clinic at Graz, but apparently he did not encounter it in Vienna although he worked there several years.

The best reviews in the American literature are by Dr. Katz[11] and later by Dr. Brown and Dr. Katz.[12]

I have seen but one patient who had what I thought was this type of dystrophy, and that was a young girl who had recurrent attacks of eczematous keratitis starting at the lower limbus until finally it spread upward as a vascular fasciculus dragging the

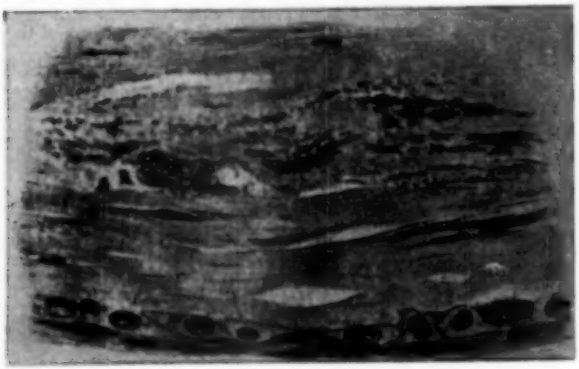

Fig. 15 (Goar). SALZMANN'S NODULAR DYSTROPHY. Section of Salzmann's case. (Reprinted with permission from Brown and Katz: *Archives of Ophthalmology*, volume 13, 1935.)

leash of vessels behind. After several years, a firm, elevated mass formed at the apex. This is very similar to Katz's case.

So far as I know only three histologic studies have been made on these nodules—those by Salzmann, Ladekare, and Brown and Katz. Their descriptions of the slides are quite different, and Brown and Katz say the reason for this is the different ages of the nodules removed. Three nodules removed by them from the same cornea gave unlike pictures, probably due to the fact that they had appeared at different dates, and the younger nodules had not reached the final stage.

Essentially the process is a degenerative change, beginning as a thinning of the epithelium with pyknosis of the cells both in epithelium and stroma, edema and vacuolation, and later hypertrophic scar formation similar to that in keloid.

This disease may be confused with the condition formerly known as Groenouw's nodular dystrophy which will be discussed later. However, it is not familial, is most often unilateral, is commonest in females, and apparently always follows phlyctenular keratitis.

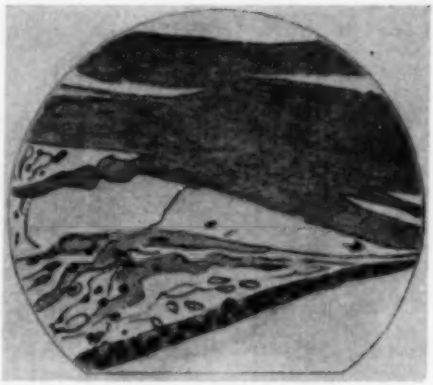

Fig. 16 (Goar). SALZMANN'S NODULAR DYSTROPHY. Ladekare's case. (Reprinted with permission from Brown and Katz: *Archives of Ophthalmology*, volume 13, 1935.)

FAMILIAL AND HEREDITARY DYSTROPHIES

It is in the hereditary dystrophies that so much confusion in regard to classification existed until recently. In 1890, Groenouw described a condition which ever since has been called Groenouw's nodular dystrophy. The same year Biber and a little later Haab and Dimmer working independently described a lattice type that has since been known as Biber-Haab-Dimmer reticular dystrophy. A few years later, Fleischer described a ringlike form which has been called Fleischer's macular dystrophy.

Most authors have thought that these dystrophies were different forms of the same disease and that a patient might show the different types as the condition progressed, also that the same family might exhibit the various types.

In 1938, Bücklers[13] published a study he had made of 129 cases, and he gave the first concrete report on the method of transmission and distribution of the lesions. Lloyd[13] seems to have made the first mention of this work in the American literature in 1939. McBain[14] from Northwestern Medical School, in reporting the case of two brothers in 1942, gave a more complete résumé of Bücklers's work.

I have found only two reports of geneal-

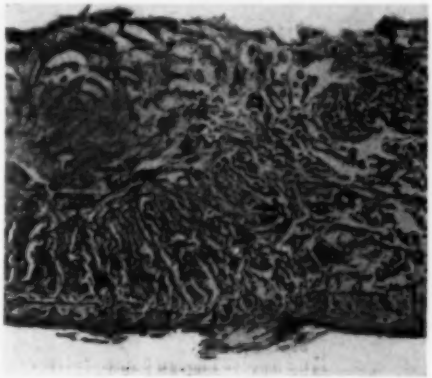

Fig. 17 (Goar). SALZMANN'S NODULAR DYSTROPHY. Brown and Katz's case. (Reprinted with permission. From *Archives of Ophthalmology*, volume 13, 1935.)

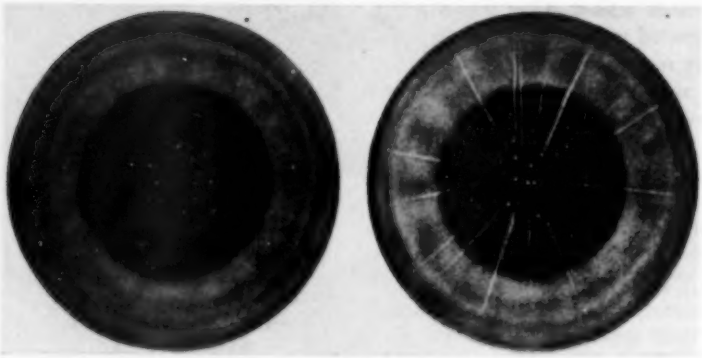

Fig. 18 (Goar). GRANULAR DYSTROPHY, early stage. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

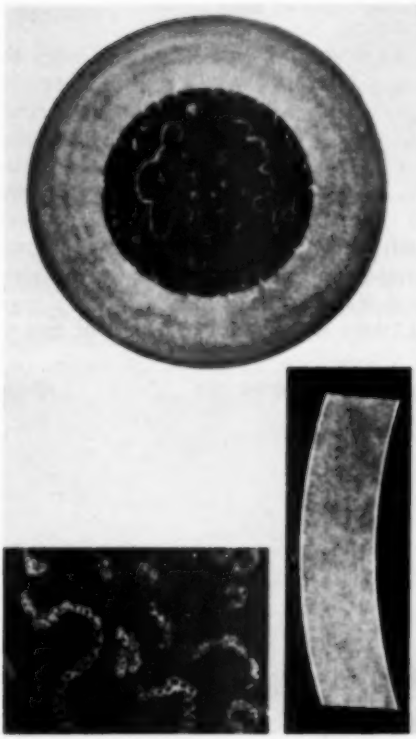

Fig. 19 (Goar). GRANULAR DYSTROPHY, intermediate stage. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

ogies of dystrophies since Bücklers's article, that of Rollet[16] in France and Mutch[19] in Scotland. Bücklers's study was fostered by the Nazi government and we shall see later that he made certain recommendations as to what should be done in attempting to improve the master race. Under totalitarian auspices, Bücklers no doubt had better opportunity for coöperation among the patients than anyone has had before or since. Bücklers concluded that there are three distinct types of hereditary dystrophies, each presenting a different clinical picture and a somewhat different prognosis. I shall discuss each briefly and attempt to point out the salient characteristics of each.

GRANULAR CORNEAL DYSTROPHY (CRUMB-LIKE OPACITY) (figs. 18, 19, and 20)

This disease is transmitted by dominant inheritance, so that it is likely to show up in each generation and half of the children be affected. However, the siblings who do not have the disease do not transmit it. It begins at an early age with small white dots in the center of the superficial corneal stroma. These dots may be connected by fine radiating lines. After several years, these lines disappear, the deposits rearrange themselves into various shapes and become

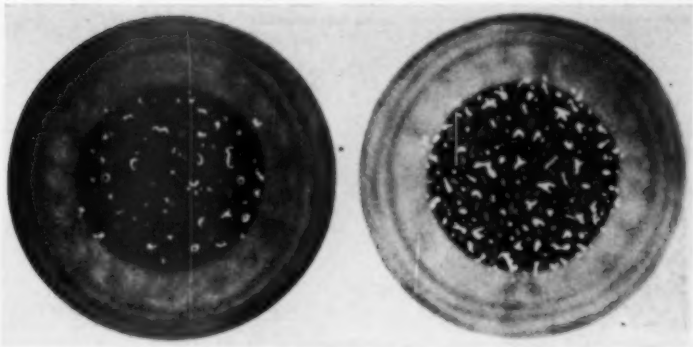

Fig. 20 (Goar). GRANULAR DYSTROPHY, advanced stage. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

heavier. With the biomicroscope they may look like fragments of stone imbedded in the cornea. There is always clear cornea between the opacities, and usually the periphery of the cornea remains clear. The superficial opacities cause elevation of the epithelium in later years, but usually it is not eroded. These people are able to see fairly well into extreme old age. This is the commonest form of hereditary dystrophy. Ninety-one of Bücklers's cases in four family trees belonged to the granular type. He recommended that marital loans be refused persons so afflicted.

Here I should like to present four cases I have observed. The first of these is Mrs.

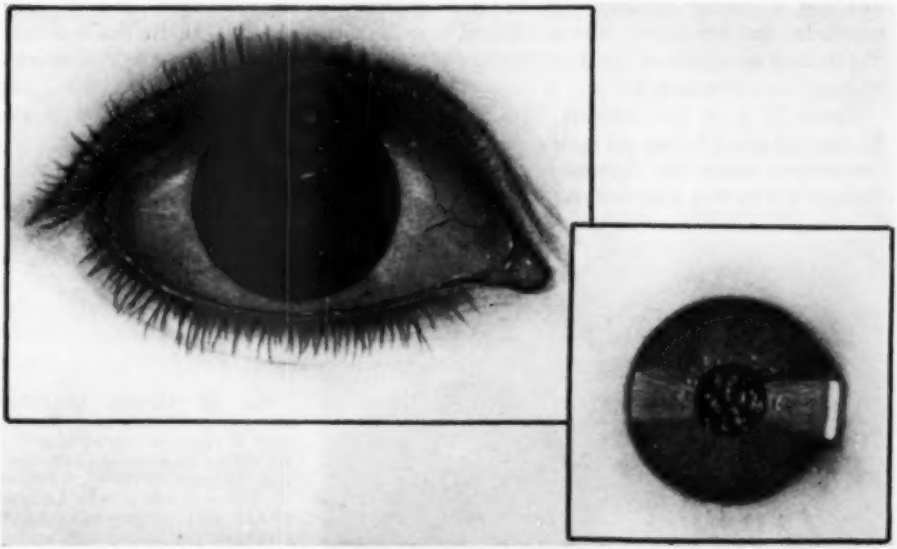

Fig. 21 (Goar). GRANULAR DYSTROPHY. (Goar's case, Mrs. H., aged 60 years.) By diffuse illumination and by sclerotic scatter.

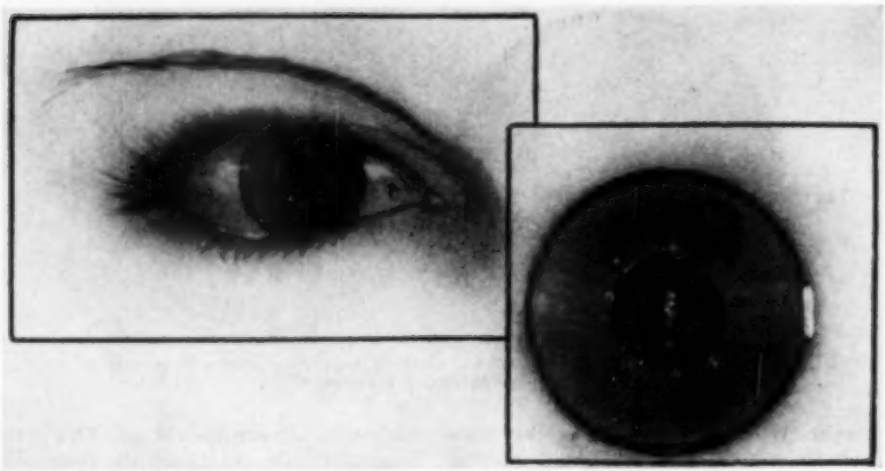

Fig. 22 (Goar). GRANULAR DYSTROPHY. (Goar's case, Mrs. R., aged 32 years, the daughter of Mrs. H.) By diffuse illumination and by sclerotic scatter.

H., aged 60 years. When she first had glasses fitted at the age of 49 years, it was discovered that she had "spots" in her corneas (fig. 21). She had two maternal aunts that had a similar condition, but had no knowledge that her mother was so affected. She has had no attacks of irritation, and her vision is normal in each eye.

Figure 22 is of her daughter, Mrs. R., 32 years of age, who has the same condition with normal vision. Her dystrophy was discovered in a routine examination.

Figure 23 is of the cornea of the right eye of Mr. H. It shows the granules to be thicker in the center, with a fine haze which resolves itself into tiny dots by the biomicroscope. This patient is aged 38 years and is the son of Mrs. H. He has been conscious of a blur in this eye for several months, and his best vision is 20/30. I was allowed to examine these cases through the courtesy of Dr. Wallace Ralston.

Figure 24 is that of Mrs. W., a 39-year-old woman. She denies that any of her

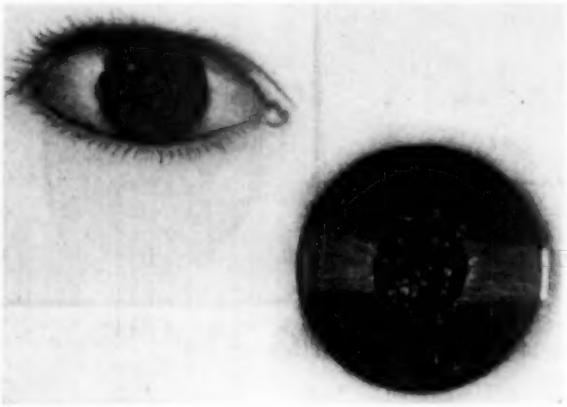

Fig. 23 (Goar). GRANULAR DYSTROPHY. (Goar's case, Mr. H., aged 38 years, the son of Mrs. H.) By diffuse illumination and by sclerotic scatter.

family has the condition. The spots look like fragments of stone in the central area, imbedded in Bowman's membrane and somewhat deeper. Her vision is normal when her myopia and astigmatism are corrected. I am unable to classify this, but it resembles the description of some of the cases of granular dystrophy.

Fig. 24 (Goar). UNCLASSIFIED DYSTROPHY. (Goar's case, Mrs. W., aged 39 years. No other member of the family was affected.)

MACULAR CORNEAL DYSTROPHY (fig. 25)

This is the second commonest type. Bücklers reported 32 cases in seven families. It is transmitted as a recessive trait, showing up unexpectedly in children of healthy parents.

Macular dystrophy appears in the first decade as a fine veil involving the whole of the cornea in the superficial layers. Within a few years, the central opacities increase rapidly in size and number so that vision is affected at an early age. Bowman's membrane is now covered in the central area by roughly circular grayish-white spots, while smaller ones appear in the deeper layers in the periphery. The cornea decreases in sensitivity, but the epithelium usually remains intact. During the fifth decade the cornea becomes so cloudy that the iris may be obscured.

These patients have recurrent attacks of inflammation but little or no vascularization occurs. Because persons with macular dystrophy become blind during the productive period, Bücklers recommended sterilization.

RETICULAR DYSTROPHY

This is the rarest of all the familial dystrophies, Bücklers reporting but six out of his 120 cases as falling in this category. It

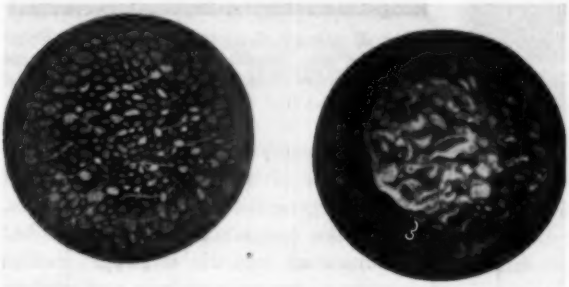

Fig. 25 (Goar). MACULAR DYSTROPHY, intermediate and advanced. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

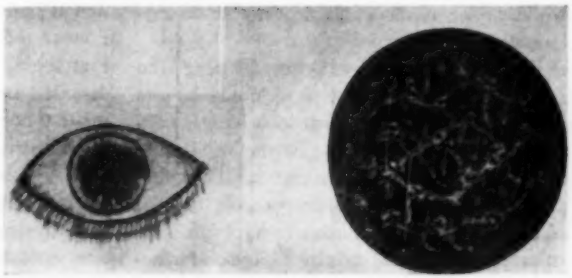

Fig. 26 (Goar). RETICULAR DYSTROPHY. (Goar's case, reported in 1930 as Groenouw's nodular dystrophy.) (Left) As it looked by oblique illumination. (Right) By diffuse illumination and biomicroscope.

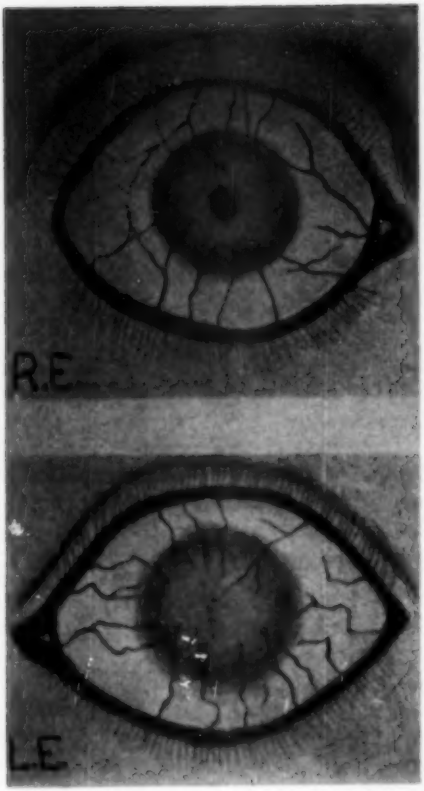

Fig. 27 (Goar). RETICULAR DYSTROPHY. (Goar's case), after a severe attack of inflammation.

is transmitted as a dominant trait. I reported a case of this in 1930 (fig. 26) as one of Groenouw's nodular dystrophy, but the picture shows that under the newer classification it is reticular. This patient underwent a violent inflammatory attack (fig. 27) while under observation, leading to vascularization of his corneas.

Reticular dystrophy begins during the second decade. The first signs noted by the biomicroscope are lines that look like threads with swellings on them, interlacing in the superficial layers of the cornea. This distribution of the lines is responsible for the old name "lattice keratitis." With the biomicroscope these threads look like solid opacities in the optical section, but by retroillumination they appear like tubules, as shown by one of Lloyd's cases (fig. 28). There is a gradual increase in thickness of the lines, and the nodules may become larger and glassier in appearance.

In the case I reported (fig. 29) these nodules were a hyalinelike substance. Attacks of inflammation occur but vascularization is rare. By the end of the 5th or 6th decade these patients are practically blind. Bücklers recommended sterilization.

Concerning the pathogenesis of lattice

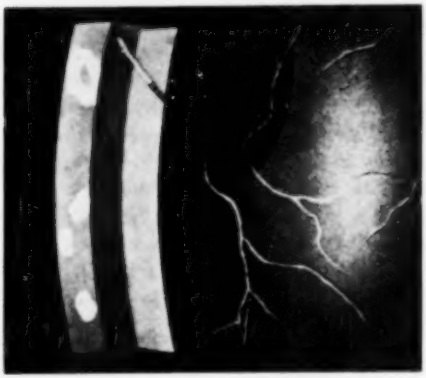

Fig. 28 (Goar). RETICULAR DYSTROPHY. (Ralph I. Lloyd's case. Reprinted with permission. From the *Transactions of the American Ophthalmological Society*, 1939.)

dystrophy, many authors have suggested that, because of its peculiar appearance, it is due to degeneration of the corneal nerves. Rollet[16] in a comprehensive paper described an edematous neuritic dystrophy which seems to fit the reticular type and suggests that it is due to inflammation and degeneration of the nerve endings. Proof is lacking that these "tubes," as Lloyd calls them, are diseased corneal nerves, and so, as in the other types of familial dystrophies, we simply return to the fact that this is a hereditary degeneration of unknown origin.

Treatment is without avail in the hereditary dystrophies except in those cases that are suitable for corneal transplantation.

Paton[17] states that Groenouw's dystrophy is suitable for corneal transplant, but does not say whether it is Groenouw's Type 1, which is the granular dystrophy, or Type 2, which is macular. As the granular type rarely reduces the vision much until old age, and then rarely incapacitates the person, it is likely that his operations have usually been on the macular or reticular varieties.

However, Von der Heydt,[18] in reporting a case of granular dystrophy that had a clear implant which began to cloud after two years remarked, "I consoled myself with the thought that dystrophy, being a hereditary characteristic, it cannot happen." It did happen though, for the transplant acquired the characteristics of the host's cornea, although vision six years after operation remained much better than before.

Fig. 29 (Goar). Reticular dystrophy. Hyalinelike nodules in histologic section. (Goar's case.)

Endothelial dystrophy (cornea guttata)

I have been interested in this condition for many years, and it was called to my attention in such a way as to leave an indelible imprint of the first case I ever recognized. Upon returning from Basil Graves's course in slitlamp microscopy, I set out to use the instrument routinely in office examinations. Soon a middle-aged woman was examined and her vision could not quite be brought to normal, although no reason for the lowering could be found.

On looking with the microscope, as the beam swept across the cornea, a great number of bright points could be seen, especially when close to the reflecting zone. The only condition I could think of that might produce this was bedewing of the endothelium, but why this should occur was a mystery to me. I suspected early glaucoma, but further examinations did not sustain this diagnosis. The patient was going to New York, so I asked her to see a distinguished colleague there. He wrote me a long letter, and it was evident that he knew just as much about it as I.

About this time an article by Basil Graves appeared in the *British Journal of Ophthalmology*,[20] entitled "A bilateral chronic affection of the endothelial face of the cornea in elderly persons." This was the first good description of the disease.

In Von der Heydt's translation of Vogt's *Atlas of Slit Lamp Microscopy* published in 1921, there is a picture showing the mosaic of endothelium with black spots in it (fig. 30). From the very brief description it appears that Vogt thought at first these holes were pits in the epithelium but later concluded they were endothelial, for he states in parentheses, "We have proven these to be the 'warts' described by Hassal and Henle."

Vogt seems to have been the first to recognize or at least to mention the condition, and later he gave it the name by which it is generally known—cornea guttata. In examining 800 eyes routinely with the biomicroscope, I gathered some interesting statistics. This condition is found more often in women, the incidence is highest in the

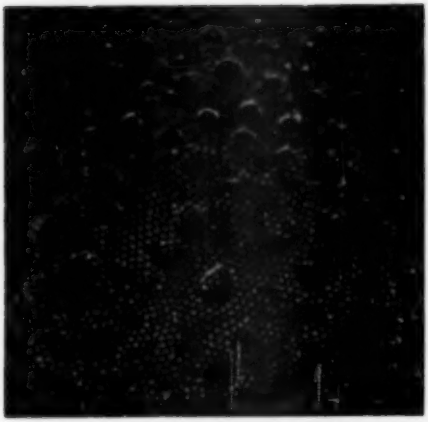

Fig. 30 (Goar). CORNEA GUTTATA. Mosaic of endothelium in axis of specular reflection with excresences. (From Vogt's *Atlas of Biomicroscopy.*)

fifth decade, and about six percent of all patients above the age of 30 years have it in some degree. No epithelial dystrophy was found in the first thousand cases examined, for I ran the series on to that figure, and, finding the percentage about the same, discontinued it.

The spangles or glints on the back of the cornea seen by focal illumination as the optical section approaches the axis of specular reflection are caused by excrescences on Descemet's membrane which protrude toward the aqueous, and their anterior surfaces act as tiny concave mirrors in reflecting the light from the slitlamp beam. Early in the disease a few of these appear in the central area of the cornea, and at this stage, if viewed in the axis of specular reflection, the warts appear as small circular black areas surrounded by a mosaic of hexagonal endothelial cells.

The condition is often progressive so that, if a young adult has it and is followed through the years, it will be noted that the following changes take place.

The excrescences become larger and more numerous until the whole central area becomes studded with them and they spread peripherally. The back surface of the cornea is now roughened, and uveal pigment granules are deposited in and between the warts. By specular reflection very few normal endothelial cells remain. By this time the vision has dropped two or three lines and cannot be improved.

Several years ago I obtained the eyeballs from an elderly patient who had been kind enough to will them to me. I thought I had the first of these eyes to be sectioned, but Vogt's new *Atlas* came out about that time and he also had sections. My sections (fig. 31) show the warts very nicely and, on histologic examination, they proved to be composed of a hyalinelike substance.

Where do these warts come from? We know that when Descemet's membrane is injured and heals, even upon reduplication, it produces nothing of this character. The warts can come only as a result of hyperactivity of the endothelial cells.

It took me some time to realize the connection between endothelial dystrophy and epithelial dystrophy of the type described by Fuchs. The endothelial dystrophy was so common and the epithelial by comparison so

Fig. 31 (Goar). HISTOLOGIC SECTION of excresences on Descemet's membrane. (Goar's case.)

rare. I do not know who first called attention to this connection, but I believe it was the Friedenwalds.[21] Kraupa[22] and Vogt[23] both found endothelial and epithelial dystrophy in the same patients, but I doubt if they realized that one is dependent upon the other.

The sequence of events is like this. Due to hyperactivity of the endothelial cells, excrescences begin to form in the central area of the cornea in a young adult. As they pile up, they eventually destroy the integrity of the aqueous barrier, and the fluid slowly enters the corneal stroma from behind. Edema of the cornea begins, and it is often possible to trace the dark lines well forward into the stroma.

Bowman's membrane (fig. 32), which is not much of a barrier to the passage of fluid, is penetrated and the epithelial cells become waterlogged. The patient now has attacks of discomfort due to exposure of nerve endings in certain areas of the epithelium. Often these areas will heal for a while and break down again upon slight provocation as in recurrent erosion. The very severe cases simulate bullous keratitis (fig. 33).

Endothelial dystrophy is always bilateral, and when epithelial involvement occurs in one eye it will sooner or later attack the other. The plight of these patients is pitiable, for not only is vision very much reduced, but in severe cases discomfort is constant. No treatment benefits them, although in the mild cases firm bandaging seems to help. In one patient on whom everything else had been tried, I was foolish enough to denude the cornea and apply iodine. It took six weeks for the cornea to recover from this insult and return to its former state. It is unwise even to put a tonometer on these eyes.

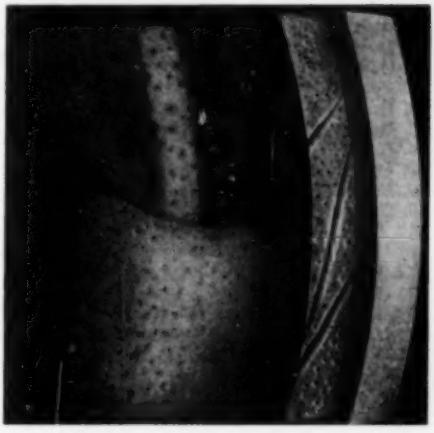

Fig. 32 (Goar). CORNEA GUTTATA, showing excresences and folds in Bowman's membrane. To the right, excresences as seen by retro-illumination. (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

Fortunately, only a small percent of the patients with cornea guttata develop epithelial changes, but one always watches apprehensively when changes begin in the 3rd or 4th decade and the excrescences increase in size and in number, and vision diminishes. Such eyes are not very good surgical risks, although I have removed cataracts in a few cases where the endothelium was extensively involved but epithelium intact, and the wounds healed without incident. This type of dystrophy is not suitable for corneal transplant as the transplant soon assumes the characteristics of the host's cornea.

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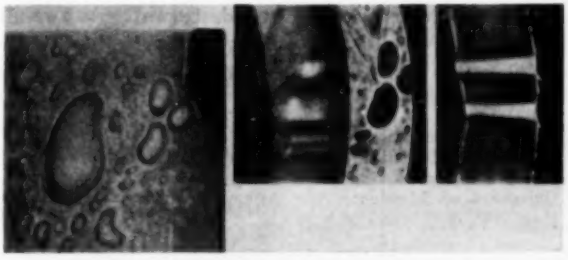

Fig. 33 (Goar). CORNEA GUTTATA with dystrophy of the epithelium (Fuchs). (Reprinted with permission from Berliner, *Biomicroscopy of the Eye.*)

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HEREDITARY AND CONSTITUTIONAL DYSTROPHIES OF THE CORNEA*

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Generally speaking, the constitutional and hereditary corneal dystrophies may be described as that relatively uncommon, or actually rare, group of ocular diseases which includes endothelial dystrophies (lesions of the posterior cornea), epithelial dystrophies (lesions of the anterior cornea), and the nodular lesions which involve the deeper corneal layers. Lesions such as herpes, neuroparalytic keratitis, dystrophies caused by vitamin and other nutritional deficiencies, and similar corneal abnormalities are conditioned by factors other than hereditary and constitutional and, therefore, form no part of this discussion. The term dystrophy, it might be well to add, implies defective nutrition but carries no implication as to the cause of the defect.

The literature dealing with hereditary and constitutional dystrophies is enormous, as well as highly confusing. A large part of it is not in English, the first investigations in this field having been made in continental Europe. A large part of it still consists of individual case reports and single observations. Although the extensive studies of certain workers, particularly Bücklers, have clarified the fundamental pathologic processes and provided a practical working classification of these lesions, all writers on the subject have not accepted his conclusions and some seem not to be familiar with them. As a result, many contributions to the literature have served to obscure, rather than to throw light upon, these special dystrophies. A further element of confusion arises from the use of eponymic terms, the usage of which frequently lacks consistency.

Actually, few comprehensive investigations of the whole question of the constitu-

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tional and hereditary dystrophies have been undertaken. One exception is the scholarly study by Franceschetti and Streiff,[1] which is based upon an unusually large personal experience, as well as upon an extensive review of the literature. Another is the somewhat similar study by Mutch.[2] Part of the value of both of these contributions lies in the extensive bibliographies which are appended and the repetition of which would be completely unjustified here.

Dystrophies affecting the whole cornea

Hereditary corneal dystrophy was first described by Groenouw in 1890,[3] and all the first reports, as well as many of the later ones, concerned experiences in the countries of central Europe. Since then, these lesions have been reported from most other European countries, from Japan, and from America, though no case, at the time of Mutch's[2] communication, had been described in a Negro.

Groenouw's[3] first report, which dealt with two patients, concerned what he called nodular corneae; Bücklers's[4] later study indicated that the first of these patients suffered from what is now known as granular dystrophy and the second from what is now known as macular dystrophy.

Biber,[5] also in 1890, put on record the first description of what is now known as reticular dystrophy. Numerous other reports were published by various observers within the next few years, and numerous difficulties were created for students of the subject, as has already been intimated, by individual vagaries of nomenclature as well as by misinterpretation of the clinical findings.

Classification

In 1938, the work of Bücklers[4] and his associate Gilch[6] resulted in an orderly classification of the corneal dystrophies. In an investigation undertaken for the German Government, under the sterilization of the unfit order, these workers carefully examined 12 family groups, consisting of 800 individuals, living in 35 small communities in Wuertemberg. Among them were a total of 129 patients suffering from some type of corneal dystrophy.

Affected patients who had previously been examined by other observers, including Fleischer, of whom more will be said later, in some instances were reëxamined and reclassified, the reclassification being comparatively easy when there were other cases of the same pedigree for comparison. This sort of investigation obviously removed the difficulties which previous workers had encountered, that of trying to diagnose and classify single instances of any special type of dystrophy.

Bücklers's[4] classification of corneal dystrophies includes three types. Of the 129 affected patients whom he studied, 91 were found to have the granular type of disease, 32 the spotted type, and 6 the latticelike type, to use the descriptive terms. His classification has been quite generally accepted, though an occasional observer still takes issue with it, or thinks that he has identified a new type of dystrophy, or contends that all three of Groenouw's types are manifestations of a single clinical entity.

Mutch's[2] review of corneal dystrophies includes an interesting outline of the classifications used by various authors, and anyone who reads it would have no trouble in understanding why one's concept of corneal dystrophies depends rather largely upon what book one happens to read. Such disagreements scarcely seem justified now.

Bücklers's investigation, however much one may deplore the reason for it, furnished the opportunity for a comparative study which the individual observer simply does not have.

Groenouw's original description of corneal dystrophy, as has already been mentioned, introduced the term nodular, although Bücklers was later able to show that one of his patients had granular and one macular dystrophy. The term nodular oc-

curs and recurs in many of the attempted classifications and that, as Mutch emphasizes, is extremely unfortunate, since the term naturally suggests that nodularity is the distinguishing feature of the condition.

Mutch also takes exception, again properly, to the use of the term keratitis in connection with corneal dystrophies. Keratitis implies the uniform presence of an inflammatory reaction; whereas, many cases have been recorded in which there had been no attacks of pain or redness at all, while in other instances attacks of inflammation were transitory and occurred after, and not before, characteristic opacities developed.

Hereditary factors

The familial character of the corneal dystrophies was first noted by Fuchs[7] in 1901. Both males and females can be affected and the disease can be transmitted through either sex. Numerous pedigrees covering several generations have been published indicating that the granular and reticular types are always transmitted in a dominant manner and that the macular type follows a recessive pattern. Descendants of healthy persons are, and always remain, healthy.

Mutch[3] properly calls attention to the fact that these statements, while generally true, require some qualification. Sporadic cases of corneal dystrophy are frequently reported, he notes, and patients with the disease have been shown at ophthalmic meetings. Brothers and sisters with the disease are stated to have healthy parents and offspring, which suggests that corneal dystrophy is not always transmitted in a dominant manner.

On the other hand, as Mutch emphasizes, unless the supposedly healthy members of the family are actually examined by competent ophthalmologists, the mere statement of a patient that there was, or is, nothing wrong with his parents' or his children's eyes must be accepted with reservations, especially as the vision of those with granular corneal dystrophy varies little from normal until they are well past middle age. Bücklers himself investigated seven pedigrees of corneal dystrophy and found that in five of them all the affected siblings belonged to one generation, no affected ancestors or descendants being found. In two pedigrees he found that one parent and several children suffered from the disease; both the grandparents and the parents in these families had married blood relatives. In some of the pedigrees studied, the blood relationship was extremely obscure and had to be traced back 8 to 11 generations, but, as might have been expected, consanguinity was present in all.

In view of the original purpose of Bücklers's investigation, it might be well at this point to state his conclusion, that compulsory sterilization of those affected with granular corneal dystrophy is not justified upon the grounds of defective vision but would be justified by the fact that this is a dominant disease, the transmission of which should be prevented by sterilization.

Granular corneal dystrophy

Granular corneal dystrophy is also known, among other names, as Groenouw's familial corneal dystrophy, Bücklers's crumblike corneal dystrophy, and keratitis nodosa. Salzmann's nodular corneal dystrophy is not the same disease; it occurs only in eyes with corneal opacities caused by previous inflammation, it predominantly affects females, and it is not familial.

Granular corneal dystrophy is a dominant disease which affects both males and females. The disease begins in the first decade and has been reported (by Saebo[8]) as early as the age of two years. It usually remains limited to the center of the cornea for many years, so that, unless the eyes are examined for other reasons, the ophthalmologist is unlikely to see the patient until there is interference with visual acuity, which is a late development.

The opacities are first seen as fine, dustlike dots, discs, or circles situated below the epithelium in the axial region of the cornea.

Somewhat later these dots form delicate, radial lines, made up of minute dots of crystalline luster. This development explains why some investigators, without the opportunity to examine many cases, have contended that the granular and latticelike types of corneal dystrophy occur in the same family and pedigree.

The radial arrangement of superficial opaque lines may sometimes remain recognizable up to the age of 30 years or thereabouts, but this is not usual. Instead, the luminescent spots increase in number and size and coalesce to form granular or crumblike opacities. The clumps, which are grayish and irregular, suggest by their outline the crumbs of bread to which they are sometimes likened. Individually they are sharply demarcated. They occupy disc-shaped areas 5 to 7 mm. in diameter, in the central region of the cornea, chiefly in the region of Bowman's membrane, though they also occur in the parenchyma as deep as Descemet's membrane. Between the particles, as well as for a marginal zone of 3 to 5 mm., the cornea is quite clear.

Franceschetti and Streiff[1] call attention to the fact that, as the crumblike opacities develop, small rings also form which, by confluence, may give the picture of an arc or a garland. Their outlines, however, remain distinct and careful examination shows that these figures are formed by the same crystalline dots as are the other opacities. Over the course of years a disclike opacity of the center of the cornea develops, which gradually increases in extent and density and which slowly assumes a deeper position.

Since visual acuity decreases very slowly, vision in youth is unimpaired and patients with this disease often retain moderately good sight up to the fifth decade in life. Even in old age vision in some cases is remarkably good. If, however, the patients are under continuous observation, it will be found that in the second decade the refraction as a rule changes, becoming astigmatic, mixed, or myopic. Correction with glasses is readily possible. Blindness sometimes develops in middle age. These different developments can perhaps be explained by regional differences, since several generations may have been affected and anticipation, according to De Cori,[9] has been observed.

In old age, the surface of the cornea is likely to become slightly irregular. Sensitivity in the majority of cases is normal.

In the absence of a familial history, the diagnosis of granular dystrophy of the cornea is frequently missed. This is particularly true in cases characterized by repeated periods of irritation with recurring erosions. Since parenchymatous alterations in the first decades of life are insignificant, the diagnosis of recurrent erosions or herpes is frequently made.

A fairly typical case of granular corneal dystrophy follows such a pattern as that reported by Attenborough,[10] in 1945. Three sisters with the disease were first seen in 1943. The eldest, aged 24 years, had experienced the onset of the condition at 18 years of age; vision in each eye was 6/9. The second sister, aged 20 years, had the onset at 13 years of age; vision in each eye was 6/24. The youngest sister, aged 14 years, had the onset at 11 years of age; vision in each eye was 6/24. Rings were present in all eyes but were most marked in those of the 20-year-old sister. The fact that the presence of the disease was not noted in the older sister until she was 18 years old is easily explained by the fact that her vision was better than that of her sisters; the opacities for the most part lay beneath the corneal epithelium and Bowman's membrane, but some were deeper in the corneal substance. Inquiry revealed the fact that the father, grandmother, and greatgrandmother were known to have had the same type of corneal dystrophy.

Von der Heydt[11] mentioned a personally observed case in which the patient had been under constant observation from her 30th to her 50th year. During this period the corneal lesion slowly progressed and her vision

dropped from 20/80 to 12/200. When she was aged 44 years, Castroviejo performed a corneal transplant.

Reticular corneal dystrophy

Reticular corneal dystrophy is also known as dystrophia corneae reticularis, latticelike corneal dystrophy, latticelike keratitis, and as Biber's, Haab's, and Dimmer's corneal dystrophy. Bücklers has emphasized that only corneal dystrophies characterized by the presence of double-contoured lines should be accepted as instances of the true reticular type of disease.

Reticular corneal dystrophy is transmitted in a dominant manner and may be apparent in the first stage of life although as a rule it is first observed at puberty. Until middle life, however, no corneal abnormality is apparent by microscopic examination. The first signs of disease consist of delicate lines in the superficial layers of the cornea, which give it the appearance of a delicate cobweb or a thin tissue or threads of glass. These opacities frequently ramify in a dichotomous manner, partly crossing each other, so that eventually a latticelike pattern results.

The opacities are situated in the anterior portion of the parenchyma or in the subepithelial layer. In their formation they raise the epithelium. In a cornea which is still transparent, though slightly clouded, small glassy, grayish, nodular or macular opacities may be seen between reticular lines which may also raise the corneal surface.

On slitlamp examination the linear opacities show double-contoured outlines, and on section they appear as delicate clefts of anterior layers of parenchyma. Nodules are found scattered all over the cornea, but linear opacities tend to lie toward the periphery. The extreme marginal zone remains free. Slitlamp examination makes clear that these linear opacities are not connected with the corneal nerves.

These opacities in their first stages were described by Haab[12] as "drops of water." Unlike granular opacities, the latticelike network present in reticular corneal dystrophy consists of channels and fissures filled with a clear substance which has a different refractive index from the surrounding cornea. Between the lines are interspersed fine, glassy, reflecting spots.

The surface of the cornea becomes irregular at an early age in this disease and corneal sensitivity is greatly diminished. As the patients grow older, both lines and nodules tend to become brownish and the lines may diminish in number and even disappear. It is fortunate that this type of corneal dystrophy is not common, for the surface irregularity produces a marked decrease in visual acuity at an early age.

Németh's[13] pedigree furnishes a good illustration of the latticelike type of corneal dystrophy. He observed the disease in a man, aged 46 years, in his 33-year-old sister, and in his two children, a girl, aged six years, and a boy, aged five years. The patient's father also had the disease; no other members of the family could be reached. The cornea in this case was described as having the appearance of scratched glass in the reflected light of the slitlamp. Macular and dotlike opacities were observed, in various depths of the substantia propria. The surface was pitted. The epithelium assumed spotted green staining with fluorescein. The cornea of the patient's sister showed the same appearance on examination, but the lesion was in a considerably earlier stage. The evidence of previous iritides in his eyes was not observed in the sister's eyes.

Both parents in this case had hyperopic astigmatism of a high degree, and the same condition was observed in both children. In, and directly beneath, Bowman's membrane, especially in the center, minute grayish-white dots could be seen with the slitlamp but not with focal illumination. Both children suffered from recurring corneal erosions.

Macular corneal dystrophy

Macular corneal dystrophy is also known

as dystrophia corneae maculosa, the recessive form of Groenouw's familial corneal dystrophy, and Fehr's macular corneal dystrophy. Kraupa's juvenile epithelial dystrophy is included by Franceschetti and Streiff in this group.

This disease is transmitted in a recessive manner, consanguinity being found by Bücklers in the seven pedigrees he investigated. It appears during the first decade of life in the form of a delicate, diffuse opacity which rapidly occupies the whole cornea. It gradually reaches the limbus and eventually occupies the whole anterior parenchymatous corneal layer. In the axial region the opacity consists of grayish spots of various shapes, larger and lighter than the spots found in the granular type of dystrophy. In the center of the cornea the dots are chiefly superficial and the cornea has a bossed, uneven surface. Near the periphery they are deeper. Isolated foci may coalesce, or may crowd together and form disclike patterns, or may remain discrete. The epithelium is often traversed by pigment lines.

In contrast to the changes observed in the dominant type of dystrophy the corneal epithelium is not greatly affected in the recessive type, but the whole surface has a dull and stippled appearance, and minute vacuoles are sometimes seen similar to those seen in acute glaucoma. Small irritating erosions occasionally occur but they are transient.

Sensitivity of the cornea may be normal or may be slightly diminished. Visual acuity becomes impaired early and by the age of 30 years the average patient is practically blind. Preservation of moderate vision for longer periods is exceptional.

Comparison of granular, reticular, and macular corneal dystrophies

Mutch[2] has given an excellent summary of the important considerations in granular, reticular, and macular corneal dystrophy. Certain characteristics are common to all three diseases: (1) The affection is bilateral, the eyes having, within reasonable limits, symmetrical opacities. (2) The onset in all three conditions occurs in the first decade of life. (3) In all, nodules cause irregularity of the corneal surface. (4) In all, vascularization is absent. (5) All are likely to be associated with attacks of pain. (6) The region of the cornea farthest from the limbus is always affected first. In the dominant forms it is the only region affected. (7) The etiology of all three types remains to be clarified. None is associated with any other known disease or defect. (8) All three types are resistant to any form of medical treatment.

The differences are stated by Mutch as follows:

1. In the granular form the opacities are irregular and discrete. In the reticular form there are interlocking lines and nodules. In the macular form the spots are so numerous as to form a diffuse opacity.

2. The opacities are located in the axial region in the granular and reticular forms. In the macular form, although they are more dense in the axial region, the whole cornea is involved.

3. In the granular form, vision remains good until middle life. In the reticular and macular forms it is impaired early in life and in the macular variety it has been reduced to finger-counting by middle age.

4. Transmission is in a dominant manner in the granular and reticular forms and in a recessive manner in the macular type.

5. Corneal sensation is good in the granular form but is defective in the reticular form and is extremely defective in the macular form.

Diagnosis

Mutch's[2] description of his own investigations, and particularly of the start of his investigation, contains a good deal of practical and useful information as to how to investigate the dystrophies. Noting that previous descriptions, on the basis of which he diagnosed his own first case, frequently did

not state whether the description was based on high or low magnification and were lacking in other respects, he undertook to evolve a diagnostic routine which would be both accurate and practical. When he realized that the pedigree was likely to be of considerable extent, and that slitlamp examination, however desirable it might be, was not practical, he found that examination with the Lister-Morton luminous ophthalmoscope with plus 20D. lens in the aperture was an acceptable substitute. The opacities could easily be seen as black shapes against the red fundus reflex. Their shapes, distribution, and number could be easily estimated and it was also easy to evaluate the status of the cornea. In the few cases in which opacities were not visible in suspected young subjects, examination with the slitlamp confirmed the negative findings.

Oblique illumination supplied by the luminous ophthalmoscope, with the battery of lenses removed, and by the binocular loupe, determined the color of the opacities and their approximate depth in the cornea. Naked-eye examination, of course, was also recorded, as were visual acuity and estimates of refraction. A careful medical history was taken, and the color of the iris was noted. Curiously, not a single case was encountered by Mutch in which an affected subject was brown-eyed.

A study of blood groups revealed no correlation between the blood group and the corneal dystrophy in any instance.

As the result of his personal investigations, Mutch concluded that the diagnosis of familial corneal dystrophy can be confidently excluded (1) if the disease is unilateral, (2) if there are signs of vascularization, (3) if the opacities are visible on naked eye examination in a patient under 30 years of age, and (4) if the same condition is not present in at least one parent.

Mutch does not share the rather general lamentation that pathologic examination is not usually practical in the corneal dystrophies. It is not possible, he remarks, to find another tissue in the body which permits as exact an examination during life of any pathologic lesion that may be present as does the living cornea. The lesions can be examined under high magnification, and the only advantage of histologic examination is the use of various stains to ascertain the nature of the opaque substance. The opacities have been thus examined by several observers, and there is general agreement that the substance is of a hyaline nature.

Therapy

As has already been intimated, the corneal dystrophies are not amenable to any form of curative treatment. This is what might be expected: The hereditary defect must be present in the germ cell, the defect developing as part of the organism and the pathologic process usually being unknown.[2] For these reasons, treatment is necessarily empirical.

Mutch's[2] list of the measures which have been advised and employed includes injections of tuberculin; iodine, mercury and potassium iodide; neosalvarsan; various chemotherapeutic agents; physical therapy; glandular therapy; superficial scraping; corneal transplantation; paracentesis; cauterization; grafting of mucosa from the lip; sympathectomy; optical iridectomy; and the use of contact glasses.

The complete lack of rationale in most of these measures is so apparent as to need no discussion. The most rational form of treatment would seem to be the maintenance of the general health, correction of the refractive error with glasses changed as frequently as necessary, and, in the occasional, carefully selected case, keratoplasty, although cases have been reported in which dystrophy attacked the graft.

Several successful keratoplasties have been reported since Franceschetti and Kiewe's first successful operation in 1936.[8] Malbrán,[14] for instance reported the performance of the perforating keratoplasty by Castroviejo's technique on two sisters

with granular corneal dystrophy. One sister recovered uneventfully. In the other, localized ectasia developed at the line of junction of the graft and the cornea, as the result of increased intraocular pressure, which subsided after paracentesis. In each case, vision improved from 1/10 to 3/10.

Hager[15] stated that he had treated two patients with the "finely dotted type of corneal degeneration described by Groenouw" (presumably the granular type) with Loewenstein's salve, a mixture of ethylmorphine hydrochloride, mercurial ointment and petrolatum album. The eyes were bandaged alternately on successive nights. From 12 to 15 diathermic treatments were also given. Vision increased in one patient from 5/18 to 5/8 and in the other from 5/6 to 5/5.

Isolated epithelial dystrophies

It has already been mentioned that during the initial stages of the dominant type of corneal dystrophy periods of irritation may occur from epithelial changes simulating recurrent corneal erosions. Occasionally a predisposition to such recurrent erosions may be dominantly inherited. This is the so-called hereditary recurring corneal erosion (disjunctio epithelii hereditaria) in which parenchymatous changes do not develop.[1]

Franceschetti[1] studied a pedigree, still unique, illustrating dominant transmission of recurrent erosions through five generations in which 32 patients were affected. He regarded these cases as significant because they illustrated that hereditary lesions can be strictly confined to the corneal epithelium.

A familial dystrophy limited to the epithelium was also observed by Pameijer:[16] The disease appeared in several members of two consecutive generations, in whom it took the form of minute epithelial vacuoles without alteration of sensitivity. A streaklike zone situated nasally below the center always remained normal.

Still another variety of isolated epithelial dystrophy reported by Franceschetti and Streiff[1] takes the form of a peculiar symmetrical dystrophy of the epithelium in which only the inferior nasal quadrant is affected. By retro-illumination in the two cases reported it was possible to determine that the cornea was apparently studded with opacities and with minute erosions such as can be seen when a small foreign body has been present under the upper lid. Occasionally the changes resembled those observed in a herpetiform affection. In both cases the sensitivity was normal.

A history of one of these cases follows:[1]

A 41-year-old man for several years had complained of acute attacks of pain in both eyes associated with considerable lacrimation, especially on waking in the mornings. All treatment had been ineffective. Vision in each eye was 20/20. The epithelial changes just described were present in both inferior nasal quadrants, but the endothelium was normal and no other abnormalities could be found. This patient, like the second patient, a 59-year-old woman, was of neuropathic constitution. Scraping of the cornea in both cases resulted in transitory improvement.

Isolated endothelial dystrophy

The disease which is best known as cornea guttata (Vogt) is also known as dewlike endothelium (Koeppe, Staehli) and the primary endothelial dystrophy of Salzmann. It is characterized by dewlike formations on the posterior surface of the cornea, which presents the appearance of a mosaic dusted over with pigment. It is best seen by retro-illumination. The overlying endothelium is rarefied or absent. The rest of the cornea is clear and sensitivity is not impaired. Examination of the guttate formations has revealed them to be excrescences of Descemet's membrane (Hassal-Henle warts).

Isolated endothelial dystrophy is not an uncommon finding in old persons and some authorities regard it as a normal senile change. It may, however, be encountered in young subjects, and it has been repeatedly observed in two generations, and in one in-

stance, by Kraupa, in three generations. It, therefore, seems reasonable to assume that it may be inherited by dominant transmission.

Combined endothelial and epithelial dystrophies

In the disease commonly known as Fuchs's epithelial dystrophy[1] the epithelium presents what amounts to a chronic edematous state, especially of the central corneal area. There is a diffuse opacity in the thickened parenchyma, and minute vacuoles, or somewhat larger vacuoles, develop in the epithelium. Droplets between the swollen cells sometimes have the appearance of glassy beads, and the composite picture is similar to that seen in glaucoma when the eyeball is under high tension. In the deeper parenchymatous layers dark lines may show dichotomous ramification. The endothelium is involved to a varying degree. Cornea guttata is also present in some cases.

Fuchs's dystrophy usually occurs in women over the age of 50 years. Clegg[17] found it in three sisters and Juler[18] in two sisters, which suggests, contrary to the views of Kraupa,[19] that hereditary transmission is a possibility.

Treatment, which consists of scraping of the cornea and painting with iodine or with aqua chlori, gives disappointing results. Vogt[20] recommended trephining, to reduce intraocular pressure, but the suggestion does not seem to have won favor.

In a case of Fuchs's corneal dystrophy reported by Ramirez[21] in a 49-year-old Negro, the condition was complicated by senile cataract. The patient, who was under observation for almost three years, complained of gradual diminution of vision and short episodes of redness and irritation of both eyes. Examination revealed the classical picture of bullous epithelial dystrophy with marked cornea guttata. Senile lens opacities developed slowly during the period of observation. Visual acuity, which was 20/200 in each eye, could be improved by contact lenses to 20/70+. These lenses were prescribed as a temporizing measure, since rapid progression and exacerbation of corneal disease have been reported following cataract operations in patients with corneal dystrophies.

Gifford, in a discussion of von der Heydt's[11] communication on corneal dystrophies, mentioned an intracapsular operation on a patient with marked dystrophy who developed, following operation, a condition which resembled Fuchs's epithelial dystrophy. Recalling that this condition does not develop until guttate lesions are so advanced that the aqueous can reach the cornea, Gifford speculated that the operation had apparently put the finishing touch on its development. Kronfeld, in the same discussion, recalled three similar cases and the question was raised whether, in such a case, one would be justified in operating for a cataract of the other eye, for fear that the same unfortunate results might occur.

Circumscribed corneal affections, without involvement of the epithelium or endothelium

Whorl opacity of the cornea[1] is a very uncommon affection which was first observed by Fleischer in a woman suffering from disseminated sclerosis. It has been observed only in women, and that it can be inherited is inferred from the cases described in a mother and daughter by Lutz[22] and in sisters by Vogels.[23]

Examination of the cornea reveals a veiled, smooth, and reflecting surface. The opacity, which is brownish, takes the form of a whirlpool, from the center of which delicate striated bundles radiate toward the corneal margin. On slitlamp examination it becomes evident that the opacity consists of single, yellowish-brown dots which are distributed throughout the cornea and which are particularly dense at the surface. The whorl appearance is the result of interfocal

gaps. When the dots are examined in reflected light they resemble refracting droplets and granules.

Since the disease is not preceded or accompanied by any inflammatory process, it may fairly be regarded as a dystrophy. Vogels[23] found glycogen in a plane section of the cornea.

Corneal sensitivity is not altered, but vision is likely to be affected. Grossly, however, the condition remains stationary or almost stationary and so can be distinguished from the transitory barrel wheel-like opacities sometimes observed in inflammation of the cornea and iris.

In 1945, Hayne[24] reported an instance of corneal dystrophy diagnosed by Gifford as Fleischer's familial dystrophy: Two brothers, aged 35 and 23 years, both suffered from failing sight, which in the 35-year-old brother had lasted for 15 years. Four sisters and the father were stated to have the same condition. The mother, a sister, and a brother had normal vision.

Uncorrected vision in the 35-year-old man was 20/200 in each eye. Ophthalmoscopic examination showed multiple densely opaque areas in each cornea. A good red reflex could be seen but the fundus details could not be discerned. With the slitlamp, large and small dense opacities were seen in the stroma of each cornea, together with numerous criss-cross lines. Neither the endothelium nor the epithelium was involved. Keratoplasty was performed on the right eye.

The 23-year-old brother showed the same corneal changes but they were less advanced. Both fundi were normal. Corrected visual acuity was 20/30 in the right eye and 20/40 −2 in the left. No treatment was undertaken. If the diagnosis was correct in these two cases, as presumably it was, this disease would seem not to be confined exclusively to females.

Biozzi and Lugli[25] described a circular peripheral density near Descemet's membrane, in the form of a band-shaped, grayish-white, double-contoured streak lying in the posterior corneal layers. In appearance it resembled folds in Descemet's membrane. It ran parallel to, and a short distance away from, the limbus. In the cases observed by these workers the fold sometimes extended up to three quarters of the corneal circumference, but the superior quadrant was never affected. Sometimes it was composed of two curves. Sometimes it was segmented or was limited to one quadrant. The outlines were always slightly wavelike and the breadth irregular, varying from 0.04 to 0.15 mm. Biozzi and Lugli were of the opinion that these streaks were actually identical with Descemet's marginal zone, which in these cases was more centrally located than usual.

This condition has been reported only by Biozzi and Lugli, who observed it three times in mothers and children, once in four siblings and once in two cousins. Transmission by inheritance thus seemed fairly evident. It bore no relationship to errors of refraction, but in two instances congenital cataract was also present, and in another case unilateral, apparently congenital ptosis was also observed.

Corneal opacities are uniformly found in the type of familial osteodysplasia known as dysostosis multiplex or gargoylism.[1] In some reported cases the opacities were suggestive of interstitial keratitis. In other reported cases the changes so closely resembled glaucomatous edema that operation was carried out, of course unsuccessfully. It was always contraindicated by the presence of normal intraocular pressure.

Under the slitlamp, according to Gasteiger and Liebenam,[26] the lesion seems to consist of numerous small, punctate, grayish-white opacities scattered over all layers of the parenchyma. At some places the spots become confluent and form larger maculas or small threads, and a reticular pattern is sometimes formed. The epithelium and en-

dothelium are unchanged. The opacities remain stationary and inflammatory signs do not occur, but visual acuity may be grossly affected. Sensitivity remains normal.

White rings in the cornea were first described by Coats[27, 28] in 1912. In this disease small rings made up of bean-shaped or kidney-shaped opacities are found, on slitlamp examination, to be composed of minute, chalk-white, distinctly limited spots. The cornea within the ring appears clear or mottled with minute dots. Sometimes chalky dots are loosely scattered over the cornea without forming a ring. They are present in all quadrants as well as in the center and vary in size from 0.5 to 1.0 mm. Slitlamp examination reveals that they lie in Bowman's membrane, which is slightly sunk or even interrupted. The corneal epithelium is intact and sensitivity is normal. The condition is usually unilateral but in the case reported by Coats it was bilateral.

The origin of this kind of dystrophy is obscure. Coats thought it was of congenital origin. Ballantyne[29] thought that it was the result of intraocular disease, which was present in all his cases. Kuan[30] advanced the theory that it arose from disease of the terminal branches of the corneal nerve, which led in turn to necrosis of Bowman's membrane, with proteic precipitation, fatty degeneration, or mineral incrustation in the periphery of the necrosed portion. The majority of observers believe that the ring originates from trauma, sometimes so slight as to pass unnoticed. It is possible that some hereditary factor will eventually be identified. Microscopic examination, which was possible in a few cases, indicates that the granules which make up the ring are composed of fat.

White rings are by no means uncommon, but they are seldom studied because, since they cause neither inflammation nor diminution of visual acuity, their discovery is usually accidental. There seems no predilection for any special period of life.

Keratitis nummularis, which was described by Dimmer[31, 32] in 1905, begins with photophobia and lacrimation. The palpebral fissure may be slightly narrowed but the conjunctiva is not usually injected. From 10 to 20 opacities are present in the cornea, irregularly scattered but chiefly near the center and only occasionally near the limbus. They are circular and dense gray. Each opacity is made up of minute dots. The foci gradually enlarge, taking the shape of circular discs, the centers of which become more densely white while the peripheral portion has a yellowish-bluish-gray tinge. Eventually the opacities may become confluent and various figures are formed and surrounded by a diffuse gray halo. The corneal surface is at first rough and mottled and later is raised and flat. Keratic precipitates, folds in Descemet's membrane in cases in which opacities were deeply situated, vascularization of the cornea, hyperemia of the iris, and iritis have all been observed.

The condition at first suggests keratitis punctata superficialis. Later it suggests disciform keratitis. Salzmann[33] was of the opinion that it was related to both diseases. Jese,[34] however, regarded it as belonging to the herpetiform group of diseases.

The disease has been reported chiefly in young agricultural workers, but has also been observed in children and old persons. The seasonal incidence, most cases beginning in August and September, suggests that external circumstances may be of some importance. Some cases appear to have been precipitated by trauma. Familial cases have not yet been reported, but since constitutional factors seem significant, the possibility of hereditary transmission deserves attention.

In keratitis nummularis sensitivity of the cornea is only slightly diminished. The course is very torpid and the disease may last for several months, but the prognosis is eventually favorable. Disturbance of vision may develop but recurrence has not been observed and complications are unusual.

Treatment is entirely symptomatic. Hot fomentations, dionine, metallic iodine and

potassium iodide have been recommended.

Summary

The group of hereditary and constitutional corneal dystrophies described in this communication are not common but must be taken into account in the diagnosis of obscure corneal lesions. They are likely to be overlooked unless the possibility of their presence is constantly borne in mind. As yet, no curative treatment is available for any of them but the patient should be kept under observation and the ophthalmologist should refrain from meddlesome interference.

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THE ACTION OF LUTAZOL AND OPHTAZOL IN THE TREATMENT OF TRACHOMA*

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Since the pathogenic agent of trachoma has not yet been discovered, the methods of treatment used up to the present time have been purely symptomatic. For the last 12 years sulfonamides have drawn the attention of research workers and especially of biologists, because of their specific action on bacteria, particularly on protoplasma.

The subject of trachoma treatment by sulfonamides has been the object of lively interest on the part of investigators. Trachoma being a chronic disease of the eyes, research workers in biochemistry have sought to develop a type of sulfonamide which would have the selective therapeutic action desired and would at the same time be tolerated by the patient. Such a drug would not produce the unwelcome secondary reactions of sulfonamides and might, therefore, be given in large doses over long periods.

A quantity of a sulfonamide known as G33† was kindly made available to us in February, 1947, by the Health Division of U.N.R.R.A., Greece Mission. Lutazol which comes in the form of two-cc. ampules of a two-percent solution or in 0.5 gr. tablets, is the sodium salt of para-sulfamido-phenyl-azo-salicylic acid, the characteristics of which are its sulfamido-azoic action and its lack of free amines. Ophtazol is the lithium salt of para-sulfamido-phenyl-azo-salicylic acid. It is obtainable as a collyrium in a one-percent solution.

Burnet, Cuenod, and Nataf, as well as Barrat, Sedan, Penau, and others, stress the very satisfactory results obtained with this drug in the treatment of trachoma and other eye diseases, such as blepharoconjunctivitis of the Morax-Axenfeld type, acute conjunctivitis of the Koch-Weeks type, hypopyon keratitis which regresses immediately upon treatment, and catarrhal and inflammatory dacryocystitis. They report that this drug has also been used with excellent results before and after various operations.

Specifically with regard to trachoma, these authors distinguish three phases in the healing process of the disease when treated with G33: (1) Quick relief from subjective symptoms—pain, photophobia, feeling of a foreign body in the eye, and profuse flow of tears. These symptoms disappear within the first few days. (2) Vascularization of the corneal pannus subsides; its infiltration begins to disappear, the cornea clears; vision improves; slight scars are left where pannus was present. (3) The action of the drug on the conjunctiva, and especially on its growths, begins to show after 3 to 4 weeks. This phase is slow to develop and, while it continues, the follicles are reduced in volume, they collapse and seem to fall on the same level with the mucous membrane or to be buried in it; finally, the follicles disappear, as well as the groups of vessels surrounding them. In general, the improvement is directed towards cicatrization.

MODE OF ADMINISTRATION

There are two successive stages in the administration of the drug: (a) the intensive stage (concentrated attack), and (b) the supplementary stage.

During the intensive stage of treatment, as applied by us, the patient is given 50 tablets of lutazol by mouth within five days; that is, 12 tablets on each of the first two days, 10 on the third, 8 on the fourth, and 8 on the fifth day. At the same time, we prescribe two drops of ophtazol locally 3 to 5

* From the Ophthalmic Clinic of the Municipal Hospital of Athens.

† G33 or lutazol and ophtazol are produced by the Roussel Laboratories.

times a day. Finally, we inject two cc. of lutazol under the conjunctiva on the 1st and 8th days of treatment.

The supplementary stage of treatment consists in giving 4 to 8 tablets daily for 2 to 3 weeks after the intensive stage has ended. The same dosage can be repeated after an interruption of 2 to 3 weeks. It should be noted that the dosage of the drug depends on both the intensity of the clinical symptoms and on the duration of the disease.

At the Howard Karagheusian Eye Clinic at Neos Kosmos, near Athens, 38 children were treated with G33 according to the method just described. Most of the patients were afflicted with Type-II and Type-III trachoma, and a very small number of them with Types III and IV (transitional period). The greater number of them exhibited corneal pannus in its initial stage at the time treatment was instituted.

This treatment was also given to 10 patients of the Ophthalmological Section of the Municipal Hospital of Athens who were afflicted with trachoma, Types II and III. In most of them pannus was present as shown in Table 1 (group 5). Five of these ten trachomatous patients had not been treated at all; and of these five, three showed corneal pannus. One of the latter had an ulcerative complication with hypopyon. The same complications were noticeable in another patient suffering from trachoma Type III.

The treatment given to the 38 children at the eye clinic lasted approximately two and one-half months. The treatment given to the hospital patients lasted about eight weeks, that is, one week for the intensive treatment, followed by two weeks' supplementary treatment, 2 to 3 weeks of rest, and a further supplementary treatment of 2 to 3 weeks.

The largest total dose given by us to the children of the eye clinic was 183 gm.; the smallest 79 gr.; the largest quantity given to them within a single month was 88 gr., the smallest 63 gr. The same dosage was applied on all children regardless of their age, (between 7 and 19 years). The same dose was also given to all the Municipal Hospital patients (age range—between 15 and 45 years).

Urine and blood tests were carried out on all patients before and after the administration of G33, in order to be able to follow more easily and in further detail the secondary action of the drug, principally as it affected the circulatory system.

Albumin, as well as hyalin and granular cylinders in measurable quantities, was detected in the urine of three children, who were on this account left out of the treatment.

Blood tests before and after the administration of the drug did not show substantial alterations. After absorption of the drug, red blood cells showed an average reduction of 230,000 units per cu. micromillimeter; white blood cells, a reduction of 5,700 units; hemoglobin, a drop of 2.7 percent; polymorphonuclear cells an increase of 1.9 percent; lymphocytes, a decrease of 3.0 percent.

Only in two cases in which high leukocytosis was at first found—15,000 (Case 36) and 8,400 (Case 17) units per cu. micromillimeter—did the count after treatment show an appreciable drop—9,000 and 4,000 respectively—thus indicating leukopenia.

In regard to the secondary effects of the drug, we observed the following: one child complained of nausea, vomiting, and pain in the hypogastrium a few days after the administration of G33 tablets. However, these symptoms disappeared as soon as the administration of the drug was temporarily suspended. Rash was noticed on the face of another child but it disappeared after a few days.

Before treatment with G33, the children had at different periods been receiving the usual treatment (silver nitrate, copper sulfate, argyrol, yellow precipitate of mercury, scarification and friction of the conjunctiva, and so forth). Only five patients—those of

TABLE 1

RESULTS OF USE OF G33 IN TREATMENT OF TRACHOMA

1.	2.	3.	4.	5.								6.		7.	8.				
Serial No.	Patient's			Duration of treatment[a] prior to Lot.-Ophtanol. Number of months patient attended clinic during years:								Type of Trachoma		Date when Lot.-Opht. treatment started	Total quantity of Lot.-Opht., in gm. taken by patient				
	Initials	Sex M. F	Age	1939	1940	1941	1942	1943	1944	1945	1946	LE	RE		Injections 1st.	Injections 2nd.	Eye-drops[c]	Tablets	Total
	GROUP I														Feb. 3	Feb. 10	Feb. 3	Apr. 24	(81 days)
1	D. A.	F	14	9	12	5					9	II–III	IV		2	2	16	161½	181½
2	N. B.	M	10		4	6				9	12	II–III	III		1½	2	17½	161½	182½
3	N. D.	F	13	10	12	10	3	8	11	12	13	III	III		2	2	17½	161½	183
4	A. G.	M	12								11	III	III		2	2	16	161½	181½
5	A. K.	F	9		4	6				2	12	III	III	Feb. 3	2	2	15½	160	179½
6	M. K.	F	10		9	5					9	II–III	II–III	1947	2	2	16	161½	181½
7	G. K.	M	17	6	6		semi-cicatrized				12	III	III		2	2	15½	156½	178
8	K. S.	F	12		12	7	2		10	12	12	III	III		2	2	16½	156½	179
9	M. S.	F	7						10	12	12	III	III		2	2	16½	161½	182
10	V. T.	F	14	6	8	6				2	11	III	III		2	2	16	160	180
	GROUP II														Feb. 25	Mar. 3	Feb. 25	Apr. 24	(59 days)
11	H. A.	M	13	9	12	6					10	II–III	II–III		2	2	12	148½	164½
12	M. A.	F	17	9	12	6					9	II–III	II–III		2	2	10½	142	156½
13	M. H.	M	15								2	II–III	II–III		2	2	11½	134	109½
14	B. K.	M	11		7	6					1	II–III	II–III	Feb. 25	2	2	11½	143½	159
15	T. T.	M	11							11	II	II		1947	2	2	11	140½	161½
16	R. T.	M	10		9	5					7	II–III	II–III		—	—	10	126	140
17	A. T.	F	9		8	11	8	12	11	12	12	II	II		2	2	12½	155½	172
18	K. T.	M	7				5	6	11	12	12	II–III	II–III		2	2	11½	154	169½
19	S. T.	F	11	1	12	10	9	12	11	12	13	III	III		2	2	12	155½	171½
20	A. Y.	F	16	8	9	7	7	3	11	12	9	II–III	II–III		2	2	11½	149½	165
	GROUP III														Mar. 3	Mar. 10	Mar. 2	Apr. 24	(52 days)
21	H. A.	F	18	[x]12	[x]12	[x]2				9	9	II–III	II–III		2	2	8½	118	130½
22	A. A.	F	18	[x]12	[x]9	[x]5				8	11	II–III	II–III		2	2	8½	109	121½
23	S. B.	F	13	9	12	6	3	5	11	12	12	III–IV	III–IV	Mar. 3	2	2	11	137½	152½
24	Y. S.	F	15	9	11	4	2	7	9	10	3	III–IV	III–IV		2	2	11	137½	152½
25	T. L.	F	15		6	6	2				10	III–IV	III–IV	1947	2	2	11	137½	152½
26	A. M.	F	14	10	12	6	5	1	10	12	12	III–IV	III–IV		2	2	11½	13.½	153
27	L. T.	F	15	9	12	9	2		10	12	12	III–IV	IV		2	2	11	13.½	152½
	GROUP IV														Mar. 17	Mar. 26	Mar. 17	Apr. 24	(39 days)
28	O. M.	M	16							3	12	II–III	II–III		2	2	8	85	97
29	A. K.	F	12			1	1	6	10	11	9	II–III	II–III		2	2	8	85	97
30	A. B.	F	17	[x]12	[x]12	[x]5			5	12	12	II–III	II–III		2	2	8	83½	95½
31	N. K.	M	13	10	12	5					9	II–III	II–III		2	2	7½	79	90½
32	V. M.	F	12	1	8	6					7	II–III	II–III	Mar. 17	2	2	8	85	97
33	M. T.	F	15	10	12	6					6	II–III	II–III	1947	2	2	8	85	97
34	A. D.	F	10			8		6	11	12	13	II–III	II–III		2	2	8	85	97
35	K. D.	F	15	9	11	5				4	12	III–IV	III–IV		—	—	7½	75	82½
36	H. T.	M	10		8	8	8	11	11	12	13	III–IV	III–IV		—	—	7	72	79
37	D. T.	F	18	[x]12	[x]12	[x]2				8	12	III–IV	III–IV		—	—	7	73½	80½
38	Y. L.	F	19		6	3					9	III–IV	III–IV		—	—	7	75	82
	GROUP V						(Municipal Hospital)								May 3	May 10	May 3	June 23	(56 days)
	(Grk. alph.)																		
39	B. X.	F	19				untreated					[x]II	[x]II		2	2	2½	67	73½
40	I. Σ.	M	24				do.					[x]II	[x]II		2	2	2½	67	73½
41	I. A.	F	39				do.					[x]II	[x]II		2	2	2½	67	73½
42	A. M.	M	45				do.					II	II	May 3	2	2	2½	67	73½
43	Δ. O.	M	38				do.					II	II	1947	2	2	2½	67	73½
44	O. Σ.	M	17				treated					II	II		2	2	2½	25	31½
45	Σ. M.	F	15				for					[x]II	[x]II		2	2	2½	25	31½
46	Γ. B.	M	14				undetermined					[x]II	[x]II		2	2	2½	67	73½
47	M. M.	M	23				length					III	III		2	2	2½	67	73½
48	Γ. H.	M	33				of time					[x]III	[x]III		2	2	2½	67	73½

[a] Column 5: excepting where sign [x] occurs, treatment consisted in curettage once every two weeks, on an average combined with calomel friction in cases of more advanced cicatrization; in between, cauterizers (silver nitrate, copper sulfate) were applied twice a week, on an average. In cases marked [x], treatment is indicated in Observations column 10.

[b] Column 9: for details of improvement observed, see body of report.

[c] Column 8: eye-drops: 15 drops to the gram.

[x] This sign is a reference to Observations column 10, same line.

the Municipal Hospital—had received no previous treatment.

RESULTS OF TREATMENT

The results obtained from the treatment of 48 trachomatous patients with G33 may be summarized as follows:

1. In noncomplicated trachoma, considerable improvement was noted after the first week of treatment in 31 out of 48 cases.

TABLE 1—Continued

9.					10.
Effects observed at successive examinations Improvement (b) = +; Condition unchanged = 0					Observations
1st. Exam	2nd. Exam	3rd. Exam	4th. Exam	5th. Exam	
Feb. 10	Feb. 17	Mar. 3	Mar. 31	Apr. 24	
+	+	+	0	0	
0	+	0	0	+	
+	+	+	0	+	
+	+	+	absent	0	
0	+	+	0	0	[a] May 3: kerato-iritis—WS test negative
0	+	+	0	0	
0	+	+	0	+	
0	+	+	+	+	
0	+	+	0	0	
+	+	0	0	+	
Mar. 3	Mar. 31	Apr. 24			
+[a]	0	0			[a] Mar. 3: ecchymosis of RE after injection
0	0	absent			
+	0	+			
+	0	0			
0	0	+			
0	absent	0			
0	+	0			
+	0	absent			
0	+	0			
+	+	absent			
Mar. 17	Apr. 1				
0	absent				[a] curettage and friction with chaulmoogra and "Cusi" antitrachomatous (mercury) ointments.
+	0				
0	0				
0	0				
+	+				
0	+				
+	0				
Mar. 31	Apr. 24				
+	+				
+	0				
+	absent				[a] same treatment as in Cases 21 and 22
+	+				
+	0				
+	0				
+	+				
+(Mar. 26)	absent				
0	0				
absent	absent				[a] same treatment as in Cases 21 and 22
+(Mar. 26)	0				
May 13	May 28	June 28			
+	+	+			[a] keratoid pannus
+	+	+			[a] keratoid pannus } on beginning treat-
+	+	pannus, hypopion healed			[a] keratoid pannus hypopion } ment
+	0	+			
+	0	+			
+	+	+			
+	+	absent			[a] keratoid pannus } on beginning treatment
+	+	absent			[a] keratoid pannus }
+	0	+			
+	+	pannus, hypopion healed			[a] keratoid pannus hypopion on beginning treatment

The remaining 17 showed no improvement. This improvement was especially noticeable in the subjective symptoms; the excessive flow of tears, photophobia, and secretions were all completely checked. As for the objective symptoms, the intense hyperemia of the bulbar and palpebral conjunctiva was reduced.

Examination of the patients followed at intervals of from seven days to three months. Slitlamp examination confirmed the improvement in the objective symptoms: the edema of the eyelids was lessened; the palpebral fissure was widened, the eyelids had become finer and their drooping had diminished; the hyperemia of the conjunctiva was reduced; the blood vessels surrounding the trachomatous growths had be-

come finer and, in many cases, atrophic; the follicles had turned pale, their volume had been reduced, but they had not disappeared.

2. The following observations were made on subjects presenting trachoma with complications: immediate improvement of the subjective symptoms, in particular after the first week of treatment, that is, after the intensive stage. Pain, photophobia, dacryorrhea, and blepharospasm had disappeared and the patients, who used to complain of pain or of the sensation of a foreign body, now felt relieved; they could open their eyes with practically no difficulty.

Of the objective symptoms, the vascularization of pannus had subsided; the vessels had become finer, leaving slight scars; and the cornea had begun to clear up.

The ulcerations of the conjunctiva were healed. Immediately after the first injection of lutazol (that is, in the course of the first week of treatment), the hypopyon showed signs of absorption—sooner, therefore, than would have been the case with the usual treatment. This improvement went on in a regular way during the second and third weeks, when keratitis disappeared entirely, ulcerations healed, leaving a slight gray scar on the cornea, and hypopyon vanished not to appear again. Moreover the eyelids showed the improvements already mentioned for the noncomplicated cases.

Summarizing the results obtained after about three months of treatment, we noted considerable improvement in both subjective and objective symptoms, but not the complete disappearance of the follicles which, as we have already emphasized, only turned pale and atrophic. Vascularization was reduced and, in many cases, disappeared. Therefore, unless the situation is changed in the near future, we would recommend that diathermic cauterization be combined with treatment with G33. This would very likely result in the full destruction of the follicles.

Regarding trachoma with complications which, as is well known, are due to a secondary infection, we consider G33 effective because it will sweep away such infection within a very short period. Disappearance of a secondary infection within one to three weeks after treatment is begun could not possibly be achieved with use of traditional therapeutic measures.

Conclusions

1. Treatment of trachoma with G33 has proved beneficial.

2. G33 has been particularly effective in complicated trachoma; corneal pannus subsides and ulcerations are healed sooner than when the standard treatment is applied.

3. In cases of secondary pyogenic infection against which G33 is active, the drug is effective.

4. G33 has a beneficial effect in all forms of trachoma, on both subjective and objective symptoms: however, it does not effect a complete cure. We have not observed, up to now, the complete disappearance of the trachomatous follicles.

5. The treatment of trachoma should therefore combine diathermic cauterization for the eradication of the follicles with the administration of G33 for shortening the period of treatment.

6. G33 is tolerated to a high degree. No dangerous secondary action of the drug has been observed.

7. Taking into consideration the fact that the largest quantity of G33 administered by us within two weeks has been 183 gm., G33 has proved to be the best tolerated of all sulfonamides which have been tried to date.

Rue Chateaubriandou et Socratous 52.

EXPERIMENTAL STUDY OF THE RETICULO-ENDOTHELIAL FUNCTION IN THE EYE*

WITH SPECIAL REFERENCE TO ITS ROLE IN THE CHEMOTHERAPEUTIC ACTION OF THE SULFONAMIDES

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The first data referring to the reticulo-endothelial function of the eye were published by Goldmann. He injected, in accordance with Ehrlich's suggestion, pyrrol blue in white mice subcutaneously and found that the connective-tissue cells containing the dye, that is, the pyrrol cells as he called them, were identical with Maximow's sessile migrating cells, Renaut's "cellules rhagiocrines," Ribbert's carmine cells, Marchand's adventitia cells, and Ranvier's clasmatocytes. Out of these pyrrol cells a high number could be found in the conjunctiva, iris, sclera, and ciliary processes. Similarly, Rados found these cells everywhere in the eye except the cornea, the crystalline lens, and the retina. Further, he has stated that, in case of inflammation, they are present also in the cornea while their number in the uvea and conjunctiva increases.

Schnaudigel demonstrated pyrrol cells after the administration of trypan blue and described the diffuse blue stain of the eye. Suganuma stained the stroma cells of the cornea with carmine injected subconjunctivally. Cucchia, Castello, and Scullica found large masses of the cells stained with carmine in inflammatory processes. Löhlein has pointed out that these cells are not present in acute keratitis because the cell proliferation observed in the first days of experimental keratitis is due to immigration of white blood cells the majority of which are polymorphonuclear cells with eosinophil granulation.

The participation of the histiocytes which can be recognized by staining the specimens with vital dyes cannot be demonstrated in the infiltrations of the cornea within 40 to 50 hours. Also Albrich has stated that neither sessile nor mobile migrating cells nor monocytes are present in the normal cornea. Thus their presence is invariably due to immigration. The main avenue of immigration is the loose subconjunctival tissue lying close to the cornea, in which histiocytes are contained in a great number, as well as the pericorneal vessels. A less important entry is represented by the anterior and posterior surface of the cornea especially in case of ulceration.

In accordance with these results, L. Németh found histiocytes in intensive keratitis; whereas, in mild suppurations they were absent. If the inflammation is intensive, the immigration of the histiocytes into the cornea can be observed as early as on the third day (after 72 hours).

First, in the center of the cornea there are leukocytes only, then the number of the histiocytes increases rapidly. On the 4th to 5th day the histiocytes are in overwhelming majority and surround the suppuration. At first they are visible as a blue ring with the slitlamp, later with simple inspection. In a later stage of the inflammation, during the repair, the histiocytes supply the proliferating connective tissue with nutriment and they dispose of the waste material consisting of destroyed cells, tissue fragments, and dead bacteria.

With regard to the manifold and extensive role of the reticulo-endothelial apparatus of the eye, especially in combating infections, the presumption seems quite natural that it plays a prominent part in the sulfonamide action. It is unlikely that the reac-

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tions preceding the chemotherapeutic effect are identical with those observed in a test tube; no doubt, the processes occurring in the living organism are much more complicated.

The sulfonamides are chemical compounds of strong reacting capacity. It is unlikely that their action is confined exclusively to the microörganisms. It is fair to assume that they exercise at least a transient influence upon the chemical reaction of the organism. The results of Tomai who observed, in human and rabbit eyes, a mild shift to alkalinicity of the pH of tear and aqueous after sulfonamide administration speaks in favor of this assumption.

The chemical action of the sulfonamide is probably associated with a secondary effect manifested in the stimulation of the reticulo-endothelial apparatus. This opinion is favored by the results of Dóczy and Horváth. These authors injected streptococci and staphylococci in rabbits and guinea pigs and examined the appearance of the phagocytes. In the animals treated with Congo red prior to the infection, the phagocytes occurred in a considerably lesser number than in the controls. Since their report is the only paper in this country in which the action of the sulfonamides following elimination of the reticulo-endothelium has been discussed, similar experiments would seem to be justified, all the more since, to our knowledge, not a single paper reporting on similar investigations concerning the eye has been published.

An elective paralysis of the reticulo-endothelial apparatus can be achieved with a 0.06-percent solution of electrocolloidal copper (Jancsó). Former methods, such as the injection of India ink, iron salts, cholesterin, trypan blue, carmine, and so forth, resulted in the blockade of the apparatus. It was, however, doubtful whether the cells definitely lost their functional ability and viability. The electrocolloidal copper proved to be an elective poison of the reticulo-endothelium of rats, its terminal effect being necrosis. The same is the case with rabbits as seen from the experiments of Paschkis.

Intravenous injection of electrocolloidal copper results in a real paralysis of the reticulo-endothelial apparatus and adequate doses are capable of destroying the whole system of the Kupffer cells and the storage cells in the spleen and bone marrow. This effect has been demonstrated by Jancsó in functional experiments and histologic examinations. The selectivity of the copper effect may be seen from the fact that the function of the liver does not fail, though the destruction of the Kupffer cells is complete. The destroyed Kupffer cells are replaced by new ones in a few days by regeneration.

My experiments published in detail in 1943 have shown that energetic sulfonamide administration is an efficient therapy in experimental suppurations of the cornea. The efficiency of chemotherapy could be increased by repeated punctures. The importance of the reticulo-endothelial system in combating the infection has been sufficiently evidenced by the examinations of Albrich and Németh. Therefore, I wished to repeat my earlier experiments demonstrating the effectiveness of the sulfonamide therapy associated with repeated corneal punctures, after the elimination of the reticulo-endothelial apparatus with Jancsó's method.

Experimental procedure

The rabbits employed in the experiments weighed three Kg. on an average. Suppuration of the cornea was elicited by hemolytic streptococci. After local anesthesia (pantocain) 0.05 cc. of a 24-hour broth culture was injected into the subepithelial space near the medial limbus of the right corneas of 16 rabbits. In the left eyes the culture was injected directly into the iris. Prior to the infection, eight rabbits were given about 2.5 cc. of Hyeden's 0.06 percent electrocolloidal copper solution into an ear vein. Then the rabbits were divided in four groups of four animals.

Group 1. The treatment consisted of albu-

cid (sodium sulfacetimide) administration and punctures.

Group 2. Puncture, no albucid (control).

Group 3. Colloidal copper, albucid, puncture.

Group 4. Colloidal copper, puncture, no albucid (control).

Within 24 hours after the inoculation, the rabbits developed a circumscribed suppuration or ulcer in the right eye and a severe iritis in the left eye. The iritis was so severe that in many cases it had to be considered an

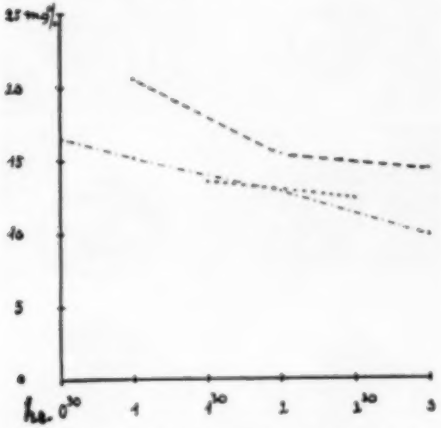


Fig. 1 (Lugossy). Concentration of albucid in the aqueous. ------, in the first aqueous; ----, in the second aqueous; ...., in the third aqueous.

endophthalmitis rather than iritis. In the animals treated with colloidal copper, the conditions were in both eyes markedly worse. Administration of albucid was started 24 hours after the infection.

On the first day, the rabbits were given, in the morning and in the afternoon, 0.5 gr./Kg. body weight by mouth and 0.3 gr./Kg., intravenously. On the second and third days, the afternoon doses were omitted. The concentration of the albucid in the aqueous of the right eye was estimated on all of the three days. On the first day the estimation was repeated with the second aqueous and in some rabbits with the third aqueous (fig. 1). On the second and third days, the second and third aqueous were not examined (figs. 2 and 3).

In order to obtain a histologic picture of

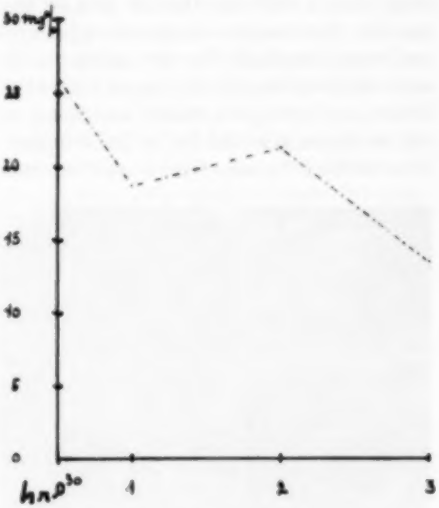


Fig. 2 (Lugossy). Concentration of albucid in the aqueous.

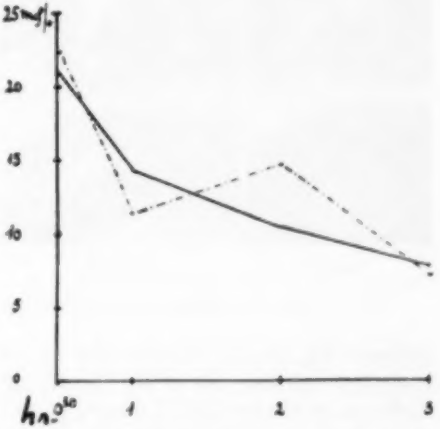


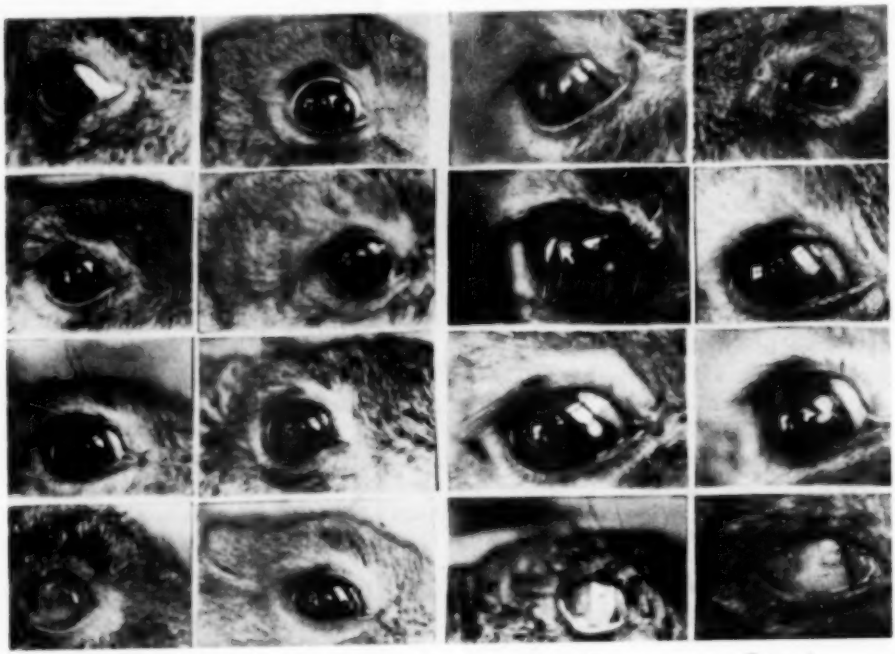
Fig. 3 (Lugossy). Concentration of albucid in the aqueous and blood. ----, in the aqueous; ——, in the blood.

the various stages of the inflammation in the different groups and to examine the cells taking part in the process one rabbit of each

group was killed every eight days. Prior to this, for 2 to 3 days, 10 cc. of a one-percent trypan-blue solution was injected intravenously once a day into the ear vein of the animals. These injections represented a serious strain, especially for the rabbits which were treated with colloidal copper before the infection, so that most rabbits succumbed to this treatment after the 2nd or 3rd injection. Nevertheless, the use of the trypan blue was indispensable for the representation of the reticulo-endothelial cells in the two groups receiving no electrocolloidal copper, as well as in the two groups treated with copper. In Groups 3 and 4 this procedure was expected to reveal whether or not the reticulo-endothelial apparatus had been destroyed by the colloidal copper solution. Since the cells destroyed by copper are replaced in a few days through regeneration, I injected one cc. of the copper solution once a week into these animals in order that the blockade could be maintained.

In Group 1, the process of healing took, apart from Rabbit 4, such a rapid course that the observations I made in 1943 could, as regards the favorable effect of energetic sulfonamide administration by mouth and intravenously, in connection with puncture, be corroborated in every respect. A good comparison could be made with the rabbits in Group 2 in which delayed healing was observed (fig. 4). The failure of the left eye to heal was striking; nearly all left eyes threatened to atrophy (fig. 5). The iritis was induced to form a basis on which the participation of the reticulo-endothelial cells could be studied.

The most instructive cases have been presented by the Groups 3 and 4 (fig. 4). Apart



Group 1 Group 2 Group 3 Group 4

Fig. 4 (Lugossy). Appearance of the right eyes of the 16 rabbits used in the experimental studies.

from the fact that the inflammation was, as compared with Groups 1 and 2, more severe, the organism of the rabbits treated with colloidal copper seemed conspicuously worn out. The rabbits became passive and had no appetite. This weariness manifested itself also in the course of the eye disease: we had the impression that the resistance of the eye tissues had been thoroughly destroyed. The conditions in Group 3 were better than in Group 4. This difference can be attributed to the simultaneous action of albucid and punctures. The chemotherapeutic compound has, in our view, accomplished its favorable bacteriostatic action independently of the reticulo-endothelial status.

The failure of the process to improve or the fact that improvement did not go beyond a temporary interruption in the disease's progress, which was followed by a continuous deterioration, and finally the delayed regeneration, were certainly due to the deficient resistance and healing tendency; that is, to the elimination of the reticulo-endothelial apparatus. The difference is especially striking if this group is compared with the quick repair exhibited by Group 1. In this group possessing an intact reticulo-endothelial system, the bacteriostasis brought about by albucid was immediately followed by regeneration and restoration.

The histologic results are in full accordance with the clinical course. In the 1st and 2nd group the animals soon developed an infiltration made up of polymorphonuclear leukocytes in the right eyes at the site of infection. The infiltration was followed by the decomposition of the leukocytes, and the process of absorption and repair was induced by histiocytes derived from the healthy tissue.

In three eyes belonging to Group 1, regeneration did not take more than one week. Later, the number of the cells containing trypan blue gradually decreased in the cornea. In the 2nd group, the process took a similar course. There was, however, a delayed repair to be observed in comparison with the 1st group treated with albucid.

In contrast to Groups 1 and 2, in the 3rd and 4th group cells containing trypan blue could not be found around the ulcers for a long time. The destruction of the ulcer in the 3rd group treated with the drug was less rapid than in the control group. Following the iris infection imposed on the left eyes in Groups 1 and 2, an abscess occurred in the vitreous body which was surrounded by a ring composed of polyblasts containing trypan

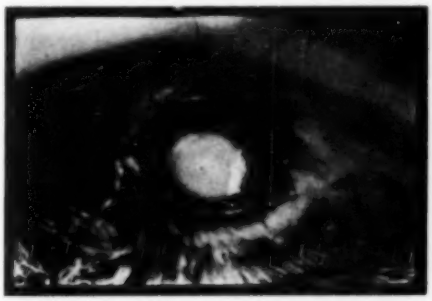


Fig. 5 (Lugossy). A left eye, showing endophthalmitis.

blue. In Groups 3 and 4 only diffuse suppuration and rapid atrophy of the eyeball could be observed.

Thus it is beyond any doubt that the chemotherapy of infections is, as Schlossberger and Maher put it, no inner disinfection but a curative process in the first stage of which the pathogenic agents are primarily impaired by a suitable drug; whereas, in the second stage they are being killed and removed by the body.

There are still numerous problems to be solved. The inference may be admitted that the sulfonamide exerts a primary damaging effect on the infectious agents; further that the defensive powers of the body contained in the blood, serum, and reticulo-endothelial apparatus have much to achieve before the agents of infection are destroyed.

It is for this reason that Domagk considers the sulfonamide action a support of the natural healing processes whereby the body

will be able to kill the microörganisms. Therefore, sulfonamides should be administered before the natural defensive power has been used up.

Summary

Streptococcus hemolyticus was used to induce corneal ulcers in the right eyes, and iritis in the left eyes of 16 rabbits. Depending on treatment, four rabbits were placed in each of four groups.

Treatment was as follows: Group 1, albucid and puncture of the cornea; Group 2, puncture of the cornea (control group); Group 3, electrocolloidal copper, albucid, and puncture of the cornea; Group 4, electrocolloidal copper and puncture of the cornea (control group).

Chemotherapy was effective, irrespective of the condition of the reticulo-endothelial apparatus.

These results show that sulfonamide exerts a primary effect on cocci in the body, and also that, before the cocci can be fully destroyed, the body, through the blood, sera, and reticulo-endothelial system, has to perform a difficult task.

II., Zsigmond u. 17-19.

My thanks are due to Professor Jancsó for his valuable advice which was a useful guide to my experiments.

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Ophthalmic Miniature

But we meet with slighter degrees of color-blindness, where the perception of red is not entirely wanting, but only considerably diminished; so that, for instance, an intense or strongly illuminated red can be perceived as such, while a less intense red appears green. A proof of this I saw at the last year's Exhibition, in a picture which represented a cattle market. The roofs of the surrounding houses were all painted red on the sunny side, green in the shadow; but—what particularly struck me—the oxen also were red in the sun, green in the shadow.

R. Liebreich, *Effects of Faulty Vision in Painting*, 1872.

THE SULFONAMIDES AND PENICILLIN IN TRACHOMA*

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INTRODUCTION

In view of the recent advances in therapy with sulfonamides and antibiotics, it seemed advisable to make a survey of their effects in the treatment of trachoma. To this end, sulfanilamide, sulfapyridine, sulfathiazole, sulfadiazine, albucid (sulfacetimide), sodium sulfacetimide (albucid soluble), Combisul (sulfadiazine, sulfamerazine, and sulfathiazole combined), Gantrisin (or NU-445, numerical designation of a new sulfonamide by Hoffman-La Roche), penicillin and bacitracin were put to clinical trial and the results observed in a series of over 3,000 patients at the Missouri Trachoma Hospital during the period 1941 to 1948, inclusive.

Some of the sulfa drugs were used in tablet form for internal medication, and some were used in solution as drops for local instillation into the conjunctival sac; the usual form of procedure being a combination of both local and internal medication concurrently. Penicillin, was instilled locally in the form of drops and also given in ointment form for overnight medication.

The advent of a new therapeutic agent is usually received with high expectation, and the sulfonamides and penicillin were no exceptions. They have proved their usefulness and assumed their place as worth-while medicaments. In ophthalmology, they have served their purpose well, notably in staphylococcic infections of the eyelids, eyeball, and lacrimal apparatus; in streptococcic, pneumococcic and gonococcic infections; and in Koch-Weeks, Morax-Axenfeld, and many pyogenic or mixed infections.

Trachoma, however, is a chronic disease which is fairly resistant to treatment generally; it is caused by a small virus or rickettsial body (Prowazek's cell inclusions) and produces a prolonged period of illness wherein the end-point is not well defined. If unchecked, the disease will result in cicatricial complications that affect both eyelids and globe and that are not readily resolved by treatment of any kind. Moreover, the stage at which trachoma ceases to be infectious is still a factor surrounded with some doubt.

Since this disease presents etiologic, clinical and pathologic characteristics not encountered in the ordinary run of conjunctival and corneal afflictions, it seemed desirable to study these new therapeutic agents over a long period of clinical trial and use before a satisfactory evaluation of their effects and results could be made.

HISTORICAL SURVEY

Formerly, such strong, harsh reagents as silver nitrate in one- and two-percent solutions, the silver-nitrate stick, copper-sulfate solutions (0.2, 0.5, and 1 percent) and the copper-sulfate stick (bluestone) were used in the treatment of trachoma. Zinc sulfate in solutions of 0.5, 0.2, and 0.125 percent was also used to a great extent. Some of the older therapeutic agents were chaulmoogra oil, tartar emetic, quinine bisulfate, mercury perchloride, lead acetate, carbolic acid, acetic acid, glycerine, trachocid, and others too numerous to mention. Trachocid is a foreign (European) proprietary preparation containing bee-venom.

Argyrol in various strengths from 5 to 20 percent, protargol, and other silver-protein preparations of recent years enjoyed a wide popularity, but resulted more often in staining of the conjunctiva (argyrosis) than in an amelioration of the disease.

Many of these preparations, although time honored in their acceptance and use, served to irritate the conjunctiva in most

* From the Missouri Trachoma Hospital.

cases, thereby adding to the inflammation already present and further devitalizing the tissues so that they became vulnerable to the already infectious agent.

During the recent decade, it was found at the Missouri Trachoma Hospital that mild or bland treatment of heavily infected trachoma cases produced a more rapid recovery than the use of strong, harsh, or irritating reagents locally on the conjunctivas. These were newly infected cases, moderately to markedly severe, but without definite corneal destruction (ulceration), with or without pannus formation.

In some instances, it was found that such fresh or recently infected cases, though accompanied with marked granulation (follicular) of the conjunctiva and with early pannus formation, responded fairly well when put on a course of hourly irrigations with normal saline solution, without additional treatment. However, although abatement of symptoms and subsidence of infective signs followed bland treatment, recovery was slow or incomplete. Search for the ideal therapeutic agent—one that was nonirritating but at the same time possessed some specificity against the infective agent of trachoma—was continued.

Discussion

There has been considerable controversy during the past decade as to whether or not the sulfonamides have a specific effect on the virus of trachoma. The majority of investigators claim they do have a specific effect and base their claims upon clinical observations.

Thygeson[1] points out that in cases in which specific inclusion bodies were found previous to the internal administration of sulfanilamide, they could not be found after treatment with this drug. Sorsby[2] concludes from his observations that the sulfonamides are indeed specific against the virus of trachoma, and not merely against any associated secondary infection. I am in agreement with the conclusions of these investigators, and it is my opinion that further bacteriologic study will conclusively prove specificity for sulfonamides in trachoma.

When the sulfonamide drugs were first used, about 1939, at the Missouri Trachoma Hospital, it was discovered that sulfanilamide in saturated solution (about 0.7 percent) used locally provided a bland medicament which was well tolerated by the patient; one that would attack the infective agent and reduce the inflammatory symptoms and turgescence. Although falling short of being the ideal agent—that is, one that would produce rapid subsidence of infection and resolution of inflammatory signs without untoward effects, and would promote quick recovery—sulfanilamide came to be accepted at the Trachoma Hospital as the drug of choice in the treatment of trachoma. The use of such strong caustics as silver nitrate and copper sulfate was abandoned, except for their occasional use in mild solutions of about 0.20 percent, once or twice a day in conjunction with hourly instillations of zinc sulfate (0.125).

The results with sulfanilamide were generally more satisfactory than with any previous routine of treatment. Discomfort to the patient was lessened. The use of the silver, copper, and zinc preparations had caused many to complain of the "hot shots" and of the burning and stinging of the conjunctiva following such administration. Locally, the conjunctival inflammation showed early subsidence, turgescence was lessened, and photophobia improved quickly. Side effects were rare, since sulfanilamide was not used internally at this time; only occasionally a sensitive individual complained of mild reactions such as flushing of the face or mild swelling of the conjunctiva and eyelids.

Following reports in the literature that internal administration of sulfanilamide was not a safe procedure, search was begun for a sulfonamide drug that would be as efficacious as sulfanilamide, or more so, but with-

out deleterious side effects. To this end, albucid (sulfacetimide) was used experimentally, both internally (tablets 0.5 gm., 45 gr. per day) and locally in solution (saturated) as eye drops. It showed no dramatic change in therapeutic results and was discarded, after several months' use, during the summer of 1941. It was considered an agent of no greater value than the sulfanilamide already in use.

Sulfathiazole was tried next in a five-percent solution and also as a pulverized solid dropped directly into the lower cul-de-sac every two hours. The powder formed an insoluble precipitate which remained as such in the conjunctiva, and proved to be of no greater efficacy than the sulfanilamide solution (0.7 percent) used previously. Furthermore, the administration of the powder was laborious. The five-percent solution also was found to be of little value. These, therefore, were discarded for local use. For internal administration, sulfathiazole in 0.5-gm. tablet form was readily accepted, however, because of its relatively low toxicity in comparison with sulfanilamide.

At the end of 1941 and during the early part of 1942, the chosen routine in the use of the sulfonamides became: (1) Sulfanilamide saturated solution, used locally for irrigation and as drops, every two hours, in the conjunctival sac, and (2) sulfathiazole (0.5 gm. tablets) given internally, 4 to 8 tablets per day (adult dosage) for one week to 10 days, both given concurrently. For children, about half the tablet dosage was administered, depending upon age and weight. An equal amount by weight of sodium bicarbonate was taken with the sulfathiazole, for alkalinization, in every case. On this routine only an occasional drug sensitivity was encountered, consisting of nausea and headaches, flushing of the face and neck, the appearance of a skin rash, and a feeling of anxiety in the patient. These symptoms quickly disappeared upon stoppage of the drug.

Late in 1942, sulfadiazine supplanted sulfathiazole as the agent of internal medication. Preference was given to sulfadiazine because it was the less toxic drug and presented fewer allergic characteristics. It was administered in 0.5-gm. tablets, given four times per day by mouth, in dosage of 6 to 9 tablets per day, depending upon patient's weight, and became the sulfonamide of choice for systemic use in conjunction with local drops and irrigations of saturated sulfanilamide solution.

Until 1946, this procedure of treatment was found to be most beneficial in trachoma, and was adopted for general use. Over 1,000 cases* of patients hospitalized at the Trachoma Hospital, of all age groups and of both sexes have been studied so far. In early or beginning cases, in moderately and markedly advanced cases, with or without pannus, and even in late cases with cicatrization, entropion and corneal ulceration, results proved beneficial.

In the late cases, however, it has been necessary to give adjunctive treatment in the form of pontocaine, atropine, heat, cautery, and intravenous administration of typhoid (nonspecific) vaccines for the attending uveitis. To date, such supplemental treatment becomes a necessity in those cases in which complications have become destructive to the tissues of the eye, and call for immediate remedial local treatment with nonsulfonamide ophthalmic reagents.

Surgery is also indicated in various cases: entropion operations to correct the incurvation of the eyelids, epilation for trichiasis, and grattage to remove the follicular growths on the conjunctiva in order to stimulate healing and repair. This phase of trachoma treatment will not be discussed here, however, as it does not fall within the province of this paper.

During the early fall of 1946, a new sul-

* Patients seen and treated in the out-patient clinic of the hospital were not included in this survey.

fonamide solution known as sodium sulfacetimide* (Schering Corporation) was tried at the Missouri Trachoma Hospital. This was supplied originally as a 30-percent solution and afforded a greater concentration of sulfonamide solid in solution than any other type of sulfonamide. However, this high concentration was found to be too irritating for use in trachoma. Many patients complained of a burning and stinging sensation and, in many observed instances, the congestive signs of local inflammation appeared to be increased instead of decreased. In a number of trachoma patients, the discomfort that followed use of this drug (in 30-percent solution) became so intense that it was necessary to stop its use entirely.

After a period of several weeks' initial trial, it was decided to try sulfacetimide in solutions of 5, 10, and 20 percent. Various dilutions were used until it was found that the 10-percent aqueous dilution produced a maximum of results with a minimum of irritation to the ocular tissues. Sulfanilamide saturated solution (0.7 percent) locally was, therefore, supplanted by sodium sulfacetimide (10-percent) solution).

The effects of sulfacetimide were noted for a period of one year or more, both when used alone as local drops and irrigations and when used in conjunction with sulfadiazine tablets taken internally. We found the sulfacetimide solution (10 percent aqueous) to be very efficacious in the treatment of trachoma, even better than the regular saturated sulfanilamide solution and sulfathiazole (five-percent solution). The sulfacetimide produced more rapid subsidence of symptoms (itching, burning, photophobia, blepharospasm) and signs (redness and turgescence of the conjunctiva, active pannus, mild concomitant iritis) and shortened the usual hospitalization period of 4 to 8 weeks to 3 to 5 weeks.

In most instances, the new drug was well tolerated locally but there were occasional complaints of itching and burning, which had not been present previous to the instillation of the sulfacetimide. In these instances, the drug had to be discontinued because no improvement would follow from prolonged use and the eyes would remain reddened, inflamed and bothersome. When sulfacetimide drops were stopped, the affected cases improved on a bland treatment with physiologic saline for several days; when again treated with sulfacetimide, the same local and side reactions were observed. This occurred not only when sulfacetimide was used in conjunction with sulfadiazine tablets internally, but also when sulfacetimide was used locally by itself.

In a few individuals, marked toxicity of the drug was noted, when used locally in the conjunctival sac, with or without sulfadiazine medication by mouth. Two white men, aged 27 and 34 years, showed a marked local and general reaction after the use of this new drug. The face, neck and body became covered with an itching erythematous rash. The conjunctivas became congested, edematous, and chemotic. These patients were taken off all sulfonamide drug medication and put on saline irrigations for one week. When symptoms and signs had subsided, the sulfacetimide solution was again tried, locally, without the sulfadiazine by mouth, and there followed a recurrence of the side effects to the same degree of intensity. In other patients sulfacetimide therapy caused milder side effects, notably flushing of the face and neck.

With reference to sulfadiazine itself, previously when used by mouth in conjunction with sulfanilamide drops or instillations locally, no noxious effects that could be noted clinically had occurred. No blood-level determinations were made or hemoglobin readings determined, but degrees of intolerance

* Sodium sulfacetimide (30-percent and 10-percent solutions), sodium sulfacetimide ophthalmic ointment (10 percent), and Combisul were generously supplied by the Schering Corporation for this clinical investigation.

or sensitivity to the drug were determined only from clinical observation and subjective symptoms. Of course, one must consider that certain individuals may manifest specific drug sensitivity to one or more drugs, which, when used on others in the same given dosage, produce no side effects at all.

In the literature, one rarely finds side reactions mentioned by observers who have used the sulfonamide drugs in ophthalmology. For instance, in Kuhn's[3] report it is stated that not one single allergic reaction to sodium sulfacetimide (30-percent solution) was observed. This is difficult to understand, unless one assumes that all of the cases in this survey were of short, acute duration and, therefore, cases in which the drug was not used over a sufficiently long period (as in trachoma) to observe untoward effects. Furthermore, it may be possible that in trachoma patients there is unusual sensitivity to this drug per se.

However, the therapeutic value of sodium sulfacetimide solution (10 percent locally) in trachoma was considered to be so much greater than that of other sulfonamide drugs previously used, that it was adopted for general use at the Trachoma Hospital, in spite of the occasional side reactions manifested by some sensitive individuals. From the early fall of 1946 until midsummer of 1947, representing a 10-month period of trial, this sulfonamide was used almost exclusively in the treatment of trachoma at this hospital. The improved curative effects more than outweighed the disadvantages of occasional side reactions and local irritation to the conjunctiva.

During April, 1947, a new experimental sulfonamide preparation was introduced by Hoffmann-La Roche for clinical investigation, termed NU-445* (later named Gantrisin). This preparation was characterized by a comparatively high solubility at neutrality. This property[4] greatly reduces the likelihood of crystalluria and deposition of crystals within the urinary tract.

Gantrisin (3, 4-dimethyl-5-sulfanilamidoisoxazole) is a white crystalline powder, supplied in tablets of 0.5-gm. size for internal medication by mouth. It attacks the same general range of organisms as does sulfadiazine. The lithium salt forms a stable 10-percent solution for ophthalmic use.

This new drug (Gantrisin), originally designated as NU-445, is not only extremely soluble but has not yet been shown to give rise to any renal irritation or crystalluria, even though the drug is given in doses up to 15 gm. and more daily.[4]

It was desirable to learn if this sulfonamide would produce desirable curative effects in trachoma rapidly, without toxic side reactions caused by other sulfonamide drugs. Accordingly, a series of trachoma patients were put exclusively on treatment with NU-445, and the results noted during the 15-month period following. Over 300 patients with early, moderately advanced, and markedly advanced cases, including those with and without complications, were studied.

The new drug was used alone as drops or as instillations of the 10-percent solution in the conjunctival sac, and also in conjunction with internal medication of NU-445 tablets (0.5 gm.) by mouth.

Since the toxicity of this drug was reported[4] experimentally to be very low, the dosage in tablets by mouth was doubled that of sulfadiazine and sulfathiazole; our patients were given from 6 to 20 tablets per day per patient, depending upon age and body weight, the average adult dose being 9 to 15 tablets per day, children about half this amount, depending upon age. In markedly active cases in adults, as many as 10 gm. per day (20 tablets) for seven days were administered. From the evidence of the Hoffmann-La Roche report,[4] a blood level of 10 to 12 mg. can usually be maintained on a daily intake of 6 to 7 gm. (12 to 14 tab-

* This compound, in the form of the lithium salt, was originally released by Hoffmann-La Roche for this clinical investigation.

lets). No sodium bicarbonate was given concurrently, since the need for alkalinization was obviated due to the high solubility of the drug in pH ranges even below 7.0.

NU-445 (Gantrisin) was found to be very efficacious in trachoma, producing a fairly rapid recovery from symptoms and a subsidence of inflammatory signs within a reasonably short time (3 to 4 weeks). Mild and moderately advanced cases responded well to treatment with this drug, when used both locally and internally. Markedly advanced cases responded somewhat more slowly but after several weeks of treatment, showed definite improvement. As with other sulfonamide drugs, corneal and uveal complications necessitated the use of other ophthalmic agents, such as atropine, dionine, pontocaine, and intravenous therapy.

The outstanding feature of NU-445 was found to be its remarkably consistent freedom from toxic side effects. In the series of cases in which NU-445 was used, whether in local instillations, or in instillations combined with tablets by mouth, there were very few instances of toxicity or of side reactions, and when these occurred, they were mild. The average tablet dosage by mouth in an adult was increased gradually from 6 tablets per day to 9 tablets and then 12 tablets; later this was again cautiously increased to 15 tablets per day. In many instances, a dosage of 18 to 20 tablets per day was maintained for a period of one week.

All internal medications were given for one week; local instillations were given constantly during this one week and continued for as long as the patient remained in the hospital, the average stay usually being from 3 to 6 weeks. Of course, advanced cases with cicatricial complications required a much longer period of treatment.

About one out of four patients on NU-445 tablets complained of mild nausea and headaches after taking a dosage of 15 or more tablets per day. This began on the same day or the day following administration of the tablets and persisted until a day or two following stoppage of the tablets. No skin reaction of any type was seen, and no local ocular reaction was observed. Mild hyperpyrexia was manifested in some individuals. In children who were on one-half or less the adult dosage, no reactions of any type were noticed. However, in no case was the discomfort from nausea, febricula, or headache of such intensity as to warrant cessation of the drug.

Patients on 12 tablets or less per day did not manifest any appreciable signs or symptoms of sulfonamide reactions at any time.

The NU-445 drops (10-percent solution*) were found to be generally mild and gentle; only occasionally did any of our patients remark about discomfort from irritation or stinging when this solution was used.

During January, 1948, a new sulfonamide (Combisul†) in tablet form was introduced by Schering Corporation. Combisul consisted of equal parts by weight of sulfadiazine, sulfamerazine, and sulfathiazole, to make a combined total of 0.5 gm. per tablet. This was given in daily dosage of 6 to 9 tablets per adult, for one week, in combination with sodium sulfacetimide solution (10 percent) used locally as drops into the conjunctival sac. For a period of six months, Combisul was used experimentally on selected hospitalized patients of the Trachoma Hospital, treatment being started on admission. Recovery was fairly rapid. The efficacy of this sulfonamide was comparable to that of sulfadiazine. No noteworthy side reactions were observed, and we consider its toxicity to be minimal.

Since it seemed possible that an emollient coating of some sulfonamide in 10-percent concentration over the ocular surfaces at night while the patient was asleep would be an ideal adjunctive treatment, we used sul-

* Later changed to 4.3 percent for optimum density.

† Generously supplied for this study by the Schering Corporation.

facetimide ophthalmic ointment* (10 percent) as routine in all cases receiving sulfonamide treatment. A liberal coating was applied between the lids following the last treatment of the day; this was done once daily for as long as the patient remained on sulfonamide treatment.

Results were fairly satisfactory but somewhat disappointing in some respects because, when the ointment was used, many patients complained of irritation and itchiness during the night. In some cases it was necessary to discontinue the use of sulfacetimide ointment because the patients complained of too much discomfort. No side reactions of any kind were noted, however, from its application.

Penicillin* was used over a six-month period (1945-46) as a routine treatment on all trachoma patients of the hospital, both in early and late cases. The penicillin was given locally by instillation or conjunctival bath every two hours in the form of an aqueous solution of the sodium crystalline salt, in concentration of 1,000 units per cc. Penicillin ointment of the same concentration (1,000 units per gm.) was used overnight. A fresh solution was made up each morning and kept under refrigeration throughout the day. A series of approximately 100 cases of trachoma was studied, including newly infected individuals and those of long-standing infection.

The results were disappointing. Penicillin has practically no effect in trachoma per se, although it shows marked efficacy in clearing up the secondary infections of Staphylococcus aureus and albus, streptococcus and pneumococcus in the eye. Cases of trachoma with concomitant blepharitis, purulent blennorrheas, and pneumococcal or staphylococcal tear-sac infections responded well and quickly to treatment with penicillin irrigations, usually within a few days, in some cases within a week. However, no improvement of the underlying trachomatous condition itself was observed to follow.

Very purulent secretions cleared remarkably within a few days. When secondary infection was the main cause of the patient's conjunctival inflammation and discomfort, penicillin relieved the symptoms and produced a rapid subsidence of inflammation. In such cases, the underlying trachoma seemed improved but this was only because the secondary infection was controlled. No sensitivity reactions were noted in any of the cases treated with penicillin.

Only surface application of penicillin was used, since it had been reported (Miller[6]) that systemic injections of adequate dosage do not produce measurable concentrations of this drug in the ocular (particularly conjunctival) tissues and fluids. Moreover, I felt that in cases of trachoma, at least, subconjunctival injections of penicillin were not justifiable, since simpler methods appeared to be as effective. Although either local or systemic subtissue injections of penicillin may be indicated in some cases of intraocular, orbital, and uveal infections, in cases of trachomatous conjunctivitis and keratitis, this form of therapy does not seem to be warranted.

Bacitracin† ointment made up for ophthalmic use, containing 500 units of bacitracin per gm. in a petrolatum base, was used in cases of trachoma over a period of several months. Bacitracin has no effect on trachoma per se, but it shows remarkable effect in clearing up secondary infections associated with trachoma. No sensitivity in patients was observed. Some purulent cases found to be resistant to penicillin seemed to yield to treatment with bacitracin, notably in chronic blepharitis of long duration, with or without ulceration.

Both penicillin and bacitracin are valuable in controlling secondary infections in tra-

* Penicillin sodium (crystalline) for use in solution was generously supplied by Commercial Solvents Corporation for this study.

† Generously supplied for this study by the Commercial Solvents Corporation.

choma and, when secondary infections are controlled, the disease itself is more readily treated with sulfonamides and the period of recovery is thereby shortened.

General results

The improvement or therapeutic effect noted from the use of the more recent sulfonamides consisted in subsidence of all inflammatory symptoms, a gradual resolution of the pannus, if early, and the rapid disappearance of photophobia and blepharospasm. In early entropion cases, there was an unfolding of the beginning incurvation of the eyelids. Cases with advanced cicatrization of the palpebral conjunctiva, causing distinct incurvation or entropion, did not respond to any treatment by medication, either locally or by mouth. In such cases, the scarring effect was so advanced as to render treatment by drug alone ineffectual.

Pannus formations

Early pannus formations are fairly well resolved by treatment with the sulfonamide drugs. Moderately advanced vascularizations, especially active ones that have invaded the cornea to some degree, will not resolve entirely. After the acute condition has subsided, however, the pannus will have a ghostlike appearance and will show thinning or fading of the vessel walls.

A well-formed pannus of greater than 3 or 4 mm. in length will respond very slowly or not at all to treatment of any kind. In such cases, treatment is prolonged and delayed, and the best that can be hoped for is a cessation of further encroachment of the vessel growth upon the cornea and a gradual thinning of the vascular twigs during recovery so that as much vision as possible is preserved.

Sulfonamide therapy will not restore the cornea to normal condition in the case of dense pannus formation. Once pannus has advanced upon the central area of the cornea, there is very little that can be done in the way of treatment to resolve or remove this invasion.

Ulceration and opacification

The same may be said of ulceration and opacification of the cornea. Treatment will not clear these conditions entirely, although some abatement can be expected. Corneal scars and ulceration respond only so far as the general condition itself improves; therefore, my experience does not permit the conclusion that sulfonamide drugs will specifically heal the corneal ulceration coincident with trachoma. Recourse must be taken to other therapeutic methods: the use of optochin (0.2-percent solution) and hot, wet dressings of boric-acid solution, hourly, being favored. When indicated, atropine, dionine, and cautery may be of help.

Some improvement of opacification (if recent) has been observed after sulfonamide treatment. Visual tests before and after treatment are an integral part of every patient's record of stay in the hospital. Unless the opacity is an old one, and well developed, the improvement in vision shown after hospitalization, although only slight, is definite. This fact convinces us that at least some resolution of corneal opacities in trachoma, whether due to pannus or ulceration does follow from treatment with sulfonamide drugs.

Never, however, have I seen a well-marked leukoma or generalized pannus formation become resolved by any sulfonamide treatment. Although a few such patients have joyfully reported that they could see better after 2 or 3 weeks of treatment, I have attributed this apparent result mostly to the effect of psychic suggestion.

Cicatrization

Once cicatrization of the conjunctiva of the lids and bulb has established itself or become advanced, there is no resolution. The improvement observed in some entropion patients under sulfonamide treatment may be attributed to relaxation of blepharospastic tendencies, and not due to absorption of scar tissue. For this reason, we see many early cases of mild entropion that will improve on

sulfonamide treatment and afterward show no incurvation at all. Cases of long duration in which the inturning of the lid has been occasioned by the destructive effects of scarification will not yield to medical treatment under any circumstances. They will require surgical correction.[7]

Summary and Conclusions

Generally speaking, the sulfonamides have proven their positive efficacy in trachoma. They stand as first therapeutic choice because of their relative mildness of action and apparent specificity against the trachoma virus.

Various sulfonamide solutions, used as drops in the conjunctival sac, have proved to be more effective than tablets used alone internally by mouth. It appears that a combination of sulfonamide drops instilled locally and tablets given internally yields the best therapeutic results.

The following sulfonamides, in order of their efficacy have been used in trachoma, locally in the conjunctival sac: Gantrisin (NU-445) solution (4.3 percent), sodium sulfacetimide solution (10 percent), sulfanilamide solution (0.7 percent), sulfathiazole solution (5.0 percent) and powdered sulfathiazole. Because of their physical and chemical properties, Gantrisin and sulfacetimide solutions seemed to be ideal for local use in trachoma.

Internal medication by mouth with sulfathiazole, sulfadiazine, sulfapyridine, Combisul, and Gantrisin (NU-445) has proved to be of adjunctive value when given in combination with sulfonamide solutions used as drops. When these drugs were given internally, alone without drops, they proved to be of only slight efficacy. With regard to sensitivity reactions, sulfadiazine, Combisul, and Gantrisin showed least toxicity and were found most satisfactory.

Penicillin and bacitracin have no effect in trachoma itself, but, for clearing up secondary infections usually concurrent with trachoma, they show a marked efficacy, and thus serve to shorten the total morbidity period of this disease.

The routine of treatment that yields optimal results at the present time is: the combined use of (1) 10-percent solution of either sodium sulfacetimide or Gantrisin (NU-445) (4.3-percent solution) dropped every two hours into the conjunctival sac; (2) sulfadiazine, Combisul, or Gantrisin in adequate dosage given internally by mouth, for one week concurrently; and (3) the ointment of sulfacetimide (10 percent) applied liberally to the conjunctival surfaces overnight.

The average newly infected case of mild to moderate severity will respond with a subsidence of all inflammatory signs and symptoms of discomfort (itching, burning, lacrimation, photophobia) within a period of 10 days to three weeks. Moderately severe cases will require several weeks of treatment, usually 3 or 4. Severe cases and cases of long duration with complications will necessitate prolonged treatment, usually from one to several months. When sulfonamide treatment becomes protracted, a second course of internal medication with tablets is given at the beginning of the second month of treatment.

After six weeks of straight sulfonamide therapy, resistant cases are given an intermediate course of treatment, with silver nitrate solution (0.20 percent) early in the morning to be followed with zinc sulfate (0.125 percent solution) every two hours for the rest of the day. At this time all sulfonamide medication is stopped. This stimulative and astringent treatment is frequently given in those cases which seem to have become resistant to further sulfonamide treatment.

Corrective surgery is usually performed after the initial course of sulfonamide therapy (10 days) is completed. Even those cases which seem to indicate immediate surgery on first examination (as in marked entropion with districhiasis) usually improve somewhat when placed on sulfa treatment

until ready for operation. This procedure clears the infected area of turgescence and swelling, thereby paving the way for a cleaner operative field. It also helps to decrease postoperative discomfort.

The place of the sulfonamides in the treatment of trachoma is established. During the past decade these therapeutic agents have been used successfully for local and systemic medication, showing results that are truly remarkable. Although therapeutic agents which give speedier effects and have greater flexibility would be desirable for use in trachoma and in secondary infections concurrent with trachoma, to date the sulfonamides are superior to all other therapeutic agents, and are particularly to be preferred to the older and harsher methods of treating this disease.

Missouri Trachoma Hospital.

I wish to express grateful acknowledgement to the Schering Corporation, to Hoffmann-La Roche, Inc., and to Commercial Solvents Corporation for their generous supply of pharmaceuticals used in this clinical survey.

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FINGERPRINTLIKE LINES IN THE CORNEA

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The literature is replete with the description of various types of lines found in the cornea, many of which are present in normal corneas only to be discovered during routine examination, while others are seen in pathologic conditions such as the dystrophies and are part and parcel of the underlying pathologic process.

In 1946, during routine slitlamp examination of a patient, peculiar wavy lines, extremely fine in character, were found. They were seen best by retro-illumination and were of such a whorl-like contour as to suggest fingerprints. A search of the literature has revealed no illustration or description of such lines. Since that time, another case of like nature has been found and it was thought that a report of both cases would be of interest.

CASE REPORTS

CASE 1

History. Mrs. W. M. L., a white woman, aged 41 years, was examined in the office on October 9, 1946. Her only complaint was slight blurring of close vision. Vision was found to be 20/20 in each eye and on refraction there was no acceptance for distance, but +0.75D. sph. was accepted for reading. This was prescribed.

No other abnormality was noted other than the presence of peculiar wavy lines perceptible only with the slitlamp and best seen by retro-illumination. These lines were extremely narrow in width and paralleled each other in much the same fashion as furrows in a plowed field. They did not follow a particular curve but rather had a wavy contour simulating fingerprints. They were not

continuous but were broken at intervals, and the same picture was present no matter what portion of the cornea was examined. In general, the whorls tended to run parallel to the limbus, the convex portion facing peripheralward and the concavity, axially.

The width of each line was slightly less than the diameter of a corneal nerve of the second order and, throughout, the width appeared to remain uniform except at the terminal portion which ended in a long sharp point. The artist's drawing somewhat exaggerates the width of the lines but the whorl-like arrangement is well shown (fig. 1). Lines of similar character were present in the fellow eye.

An attempt was made to localize these lines as to depth in the cornea but this was not too accurate since the lines were poorly seen with direct illumination. As near as could be ascertained, they were located in the basal layers of the epithelium or else in the extreme superficial zone of Bowman's membrane.

Since we were not conversant with any lines of similar nature, it was felt that these lines might represent an artefact and the patient was advised to return for reëxamination in one week's time. On the return visit, and on several occasions thereafter, the lines were found to be unchanged.

Course. On December 3, 1946, the patient developed a dendritic ulcer on the right cornea. This was treated by complete curettage of the corneal epithelium followed by application of 3.5-percent iodine, 70-percent alcohol, and then 4.0-percent cocaine. Healing was complete by December 7th and it was found at this time that the lines previously noted had disappeared in the eye in which curettage had been carried out. It seemed logical, therefore, to assume that the lines had been located in the epithelial layer since it was this layer which had been curetted. It is possible, however, that the lines might have been in the superficial zone of Bowman's membrane and may thus have been removed by the curettage.

Fig. 1 (Guerry). Artist's drawing of fingerprint-like lines in the cornea. The width of the lines is somewhat exaggerated but the whorl-like arrangement is well shown.

On January 28, 1947, a recurrent dendritic ulcer appeared and the same treatment as previously employed was carried out. In addition, atropine and penicillin ointment were employed locally. The patient was hospitalized at St. Luke's Hospital. On February 10th, foreign protein in the form of intravenous typhoid was begun and streptomycin ointment was substituted locally for the penicillin. Four injections of foreign protein were carried out over a period of the next 10 days and by February 24th the lesion had healed completely, leaving a faint nebula extending from the 2- to 4-o'clock positions midway between the limbus and pupillary area. There was no staining at this time. The patient's vision was 20/30.

Consultation. On March 19th, the right eye again became red and painful and the epithelium in the nebulous portion of the cornea was found to have broken down, giving rise to a recurrent dendritic ulcer. The patient was then referred to Dr. John Dunnington, Institute of Ophthalmology, Presbyterian Hospital, New York, for consulta-

tion. He concurred in the diagnosis of a recurrent herpetic process and, after a sojourn of 10 days at the Eye Institute on routine treatment, the patient was discharged with the lesion completely healed.

While hospitalized, the patient was examined under the slitlamp by Dr. John Dunnington, Dr. Gordon Bruce, and Dr. Ludwig von Sallmann and their opinion was that the fingerprintlike lines were of no pathologic significance and were probably congenital in nature. Insofar as they were aware, no case of like character had been reported in the literature nor had they personally seen such a case. At this time, a drawing was made by Mr. Bethke (fig. 1).

Outcome. Since that time, the patient has had no further difficulty and, when examined on January 9, 1948, the vision in the right eye was +1.75D. cyl. ax. 140° = 20/20—2; and the left eye, −0.25D. cyl. ax. 10° = 20/20. A faint nebula in the region of the healed ulcer still remained. Lines were present in the left eye but none could be found in the right eye, the eye in which curettage had been carried out.

General examination and routine laboratory procedures were negative.

Case 2

History. Mr. J. S. E., a married white man, aged 65 years, was seen in the office on April 24, 1947. His only complaint was that his vision had failed slightly in the past year and he felt that he needed new glasses.

On examination, the patient's vision was found to be 20/100 in both eyes correctible to: R.E., +0.5D. sph. ⊂ −1.25D. cyl. ax. 140° = 20/20+1; L.E., +0.25D. sph. ⊂ −1.0D. cyl. ax. 30° = 20/20—2, with +1.75 add. No other abnormalities were noted except on slitlamp examination which revealed the following: Lines similar to those described in Case 1 were present in both eyes. In addition, there was early bilateral cornea guttata.

General physical examination and routine laboratory procedures were noncontributory.

Discussion

Apparently the fingerprintlike lines described are completely benign and of no significance. They may well be present from birth but they do not seem to be passed on to children. Three children of the patient in Case 1 were examined and found to show no evidence of the condition. Also one brother and two sisters of the patient in Case 1 were examined and no evidence of this condition was found.

The appearance of the fingerprintlike lines together with cornea guttata in the second case appears to be coincidental and there does not seem to be any relationship between the two conditions.

It should be noted, however, that lines of similar contour but of greater width and associated with vesicles and edema do occur in late corneal dystrophy of the Fuchs's type; or they may occur, surrounding the base of the cone, in conical cornea.

It is also conceivable that this condition might be confused with an old interstitial keratitis in which the cornea has cleared leaving vascular remnants. There should be no confusion if it is remembered that the vascular remnants in such a condition are in the deep stroma, while the fingerprintlike lines are superficial. Furthermore, the pattern of the vascular remnants is linear rather than whorl-like as seen in the fingerprintlike lines.

As to the incidence of this condition, we have no accurate figures. The two cases reported were found among 8,000 patients, most of whom received slitlamp examination.

Vogt* reports a case with illustration in which the lines superficially resemble those described in this paper. In his case the lines were located well within Bowman's membrane and were much more prominent and of considerably greater width than those herein reported.

505 Professional Building.

* Vogt, A.: Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges. Berlin, Julius Springer, 1930, v. 1, p. 265.

OCULAR PATHOLOGY OF DIABETES*

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The importance of diabetes as a cause of blindness has increased as a larger number of diabetics have survived with insulin treatment. The recent increase of the life span of the population has also increased the number of people who live long enough to develop diabetes. Present therapy with insulin and diet permits a longer life, but does not prevent the eventual development of diabetic lesions in the eyes.

In addition to the increase in blood sugar, there are metabolic disorders and tissue changes in diabetes which cause ocular damage. The time of onset of the characteristic retinopathy has only recently been appreciated. Before 1921, few diabetics lived long enough to develop retinopathy. Since the discovery of insulin by Banting and Best[1] in 1921, larger numbers have survived for many years so that we now have the data to formulate tentative figures.

A rough approximation can be made by rating the cases as mild, moderate, and severe. A severe diabetic usually develops retinopathy within eight years and a mild diabetic in 24 years; the moderate case requires between 8 and 24 years for its development. Hanum[2] states that about half of those who have diabetes for 10 years have retinopathy, and it is found in almost every case in which the disease has existed for 24 years. The reports of Waite and Beetham[3] and Hanum have shown that the appearance of retinopathy is apparently a factor of the duration and severity of the disease.

Unfortunately, although modern care with diet and insulin modifies the concentration of sugar in the blood and may prevent its appearance in the urine, it does not ward off the development of ocular complications. There must be other less obvious factors involved in diabetes that have not been defined. Poor care of the diabetes, or lack of care, probably increases the incidence of retinopathy, but even this is not proven.

Forecasting the appearance of retinopathy has many limitations. For one thing, there is great difficulty in determining the time of onset of diabetes, as many patients have it for years before they are aware of it. It is often accidentally discovered by a routine urinalysis. The ophthalmologist may even be the first to diagnose diabetes in the course of an eye examination by discovering the characteristic retinopathy, which means the patient has probably had the disease for at least eight years without being aware of it.

Many of the ocular lesions are quite different from those seen in the rest of the body. This is very unusual, and arouses speculation about its cause. Pathologic conditions involving the vascular system are the most likely basis for most of the ocular disturbances. The ocular vessels are highly specialized and different in many ways from other vessels of the body. They have special adaptations for this location and are peculiarly vulnerable to diabetes. Only the glomerular lesions in Kimmelstiel-Wilson's disease bear a resemblance to the retinal vascular changes.

More attention needs to be focused on the important eye lesions so that methods for prevention and care may be found. The outlook now seems poor, but only two decades ago it was far worse for then few diabetics lived long enough to develop ocular lesions. Undoubtedly much more must be learned of the faulty diabetic metabolism that ini-

* This study was done at Montefiore Hospital, aided by the William L. Hernstadt Fund. I am indebted to Dr. B. F. Payne for the use of his material at the New York Eye and Ear Infirmary and to Brig. Gen. R. O. Dart and Helenor C. Wilder for the use of their cases at the Army Institute of Pathology. Read in part before the New York Society for Clinical Ophthalmology, November, 1948.

tiates the eye lesions before they can be controlled.

Pathologic study

In studying the ocular pathology of diabetes, I examined sections from 110 eyes. One hundred were enucleated primarily to relieve a painful and intractable glaucoma. Ten eyes were obtained at autopsy at Montefiore Hospital. These proved to be free from the complications of glaucoma and were, therefore, of special interest. The patients had all had long-standing diabetes; the youngest was aged 28 years, but most of them were past the age of 50 years.

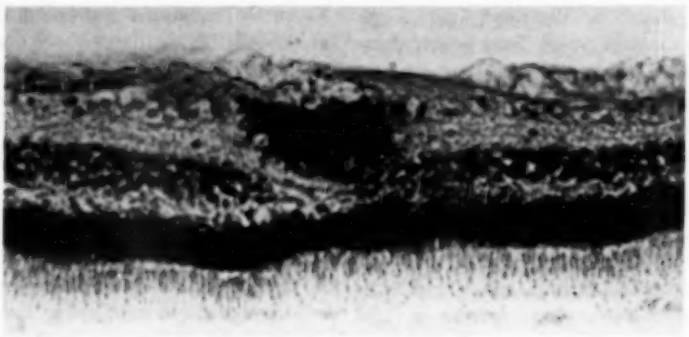

Fig. 1 (Gartner). Retinal hemorrhage.

Diabetic retinopathy

There are a number of ways in which diabetes affects the eyes. After considerable discussion, it has been generally accepted that there is a specific diabetic retinopathy which can be recognized ophthalmoscopically. It is almost always bilateral. There are changes in the retinal blood vessels, characteristic hemorrhages and exudates, mainly around the macula, and to a lesser extent about the disc.

Retinal hemorrhages are often the first definite sign. Some are as small as a pinpoint, but most are a little larger, while a few are diffuse and large. The hemorrhages are usually in the superficial layers of the retina. Larger hemorrhages may break through the anterior limiting layer of the retina and lie upon it or extend into the vitreous. Hemorrhages in the deep layers of the retina are not so common.

Parsons,[4] in his textbook of pathology (1907), noted that, in diabetes, hemorrhage from a capillary aneurysm was frequent. The common occurrence of capillary microaneurysms has been recently described by Ballantyne and Loewenstein.[5] Some of the so-called punctate hemorrhages are probably capillary aneurysms. These are not readily demonstrated by the usual histologic techniques but are beautifully demonstrated by Hotchkiss-Friedenwald[6] stain. He found the aneurysmal sacs were often incompletely lined with endothelium and took that as an indication that a break in the capillary wall occurs first, with a slow leak of blood cells, and that later the endothelium grows out to enclose the blood and form the aneurysmal sac.

A characteristic of the hemorrhages, as well as of the capillary aneurysms, is that they are usually first seen around the macula and are always more common in the zone surrounding the macula. Hemorrhages are occasionally seen in other areas around the disc, and rarely in the periphery.

The pattern of the hemorrhages slowly changes as old ones are absorbed while new ones develop. In some cases they are replaced by fibrous tissue, as may occur with

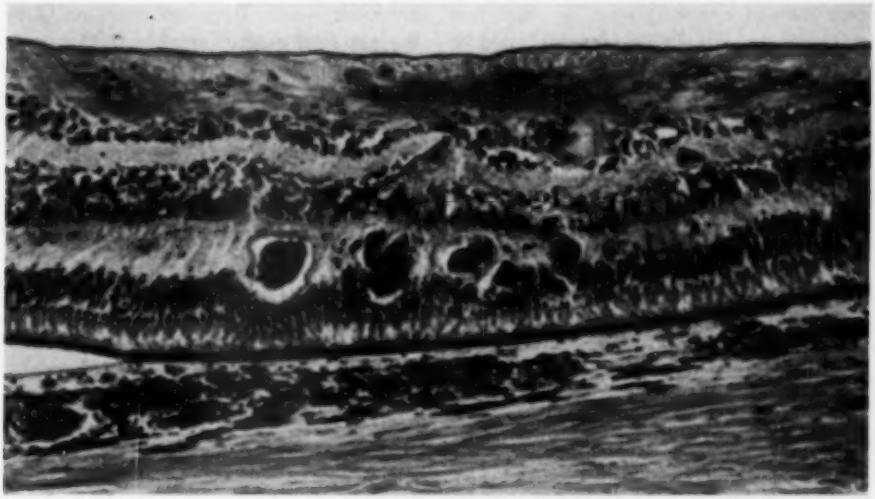

Fig. 2 (Gartner). Diabetic retinopathy. Large hyalin exudates are in the external nuclear and plexiform layers. Small lipoid exudates are in the internal nuclear layer. Degenerative changes in the inner layers were caused by previous hemorrhages.

large vitreous hemorrhages. The capillary aneurysm is usually very small, often difficult to see ophthalmoscopically, but once developed, it remains a long time.

Retinal hemorrhages are one of the early signs of diabetes and have been found in young, as well as in older persons. Givner[7] described them in a diabetic child, 12 years of age.

The exudates generally are located, like the hemorrhages, around the macula and to a lesser extent about the disc, but are rare in the periphery. The ophthalmoscopic appearance is striking. They usually have a characteristic yellow-white color with a waxy luster which is diagnostic. Frequently, there are some white exudates. The exudates are small and round and have rather sharp borders. They may be isolated, but usually occur in clusters and give the appearance of the silhouette of a bunch of grapes. The borders of a confluent mass are scalloped and consist of portions of contiguous and overlying circles.

Histologic study shows a concentration of exudates around the macula. They occur as two types. The first is found deep in the external nuclear and external plexiform layers. They are large hyalin masses with rounded edges. Although usually stained pink with hematoxylin-eosin, they occasionally take a bluish stain suggestive of calcification. This type of exudate is also found in

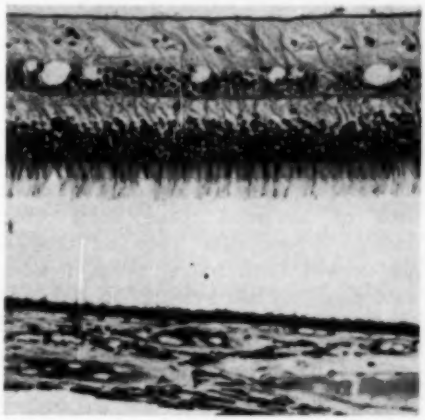

Fig. 3 (Gartner). Exudates in the internal nuclear layer are usually dissolved in preparation of the slide. This leaves cystic spaces.

some cases of arteriosclerosis, in which it is less common, usually less concentrated at the macula, and scattered around the posterior pole.

The second type of exudate is found in the internal nuclear layer with some extension to the neighboring layers. These are small exudates, often rounded, and readily lost in the usual histologic preparation, so that only a cystic space is left. These spaces may honeycomb the internal nuclear layer. The exudate takes a delicate pink stain with hematoxylin-eosin and has the appearance of serum of fibrin. The frequency with which the exudates are lost, as well as their staining characteristics, suggest a lipoid content.

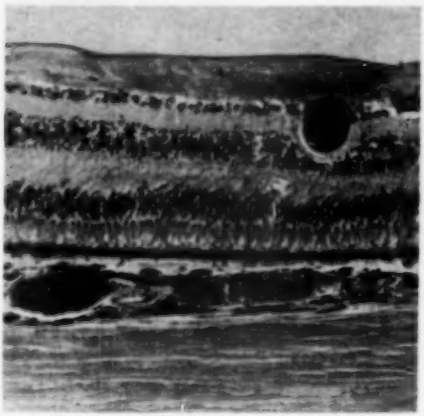

Fig. 4 (Gartner). Capillary micro-aneurysm.

The source of the exudates is not certain, but they are probably derived from collections of abnormal tissue fluids which undergo degeneration. They are probably not derived from retinal tissue. Friedenwald suggested that exudates arise through small breaks in the capillary walls which permit plasma to escape but not red cells, and as the plasma becomes inspissated, the exudate forms. The vascular disturbances of diabetes cause frank hemorrhage, so it could also allow the escape of various blood fractions which form the exudates. Once the exudates escape into the tissue spaces, absorption is slow due to the defective circulation, so they undergo degenerative changes.

Exudates are generally a feature of adult diabetes. They are rarely found in patients younger than 20 years of age, not too frequently until after the age of 35 years, after which they become increasingly common.

Capillary fragility. Studies have shown increased capillary fragility in diabetes, with a frequency which increased with the duration of the disease. Almost all patients with diabetic retinopathy also showed increased capillary fragility according to Rodriquez and Root[8] and Donegan and Thomas.[9]

The use of rutin, a glucoside derived from plants, especially buckwheat, which, by decreasing capillary fragility, has been found effective in reducing the tendency to bleed in a number of diseases, reduced the capillary

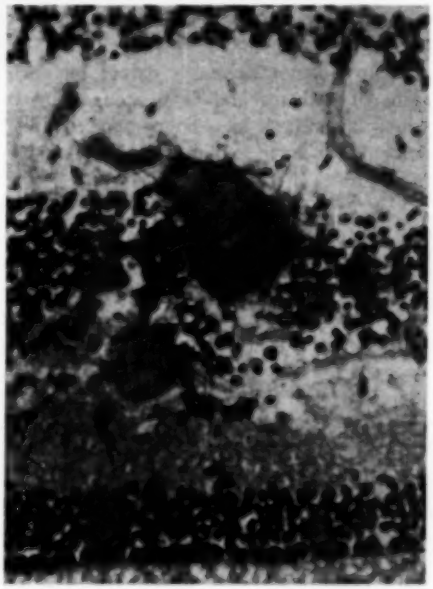

Fig. 5 (Gartner). Occluded capillary micro-aneurysm.

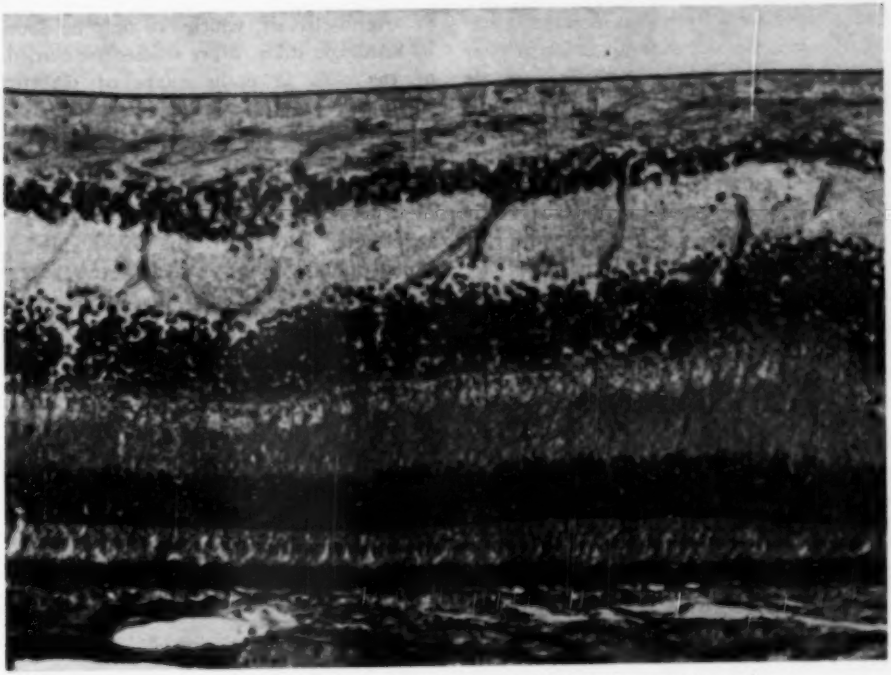

Fig. 6 (Gartner). The capillaries in diabetic retinopathy are increased in number and their lumens are dilated.

fragility to normal in these diabetics. Unfortunately, however, it did not improve the retinopathy.

The reports in the literature have been conflicting in their claims, with many authors reporting some cases that showed improvement. Larger doses of rutin, that is up to 120 mg. a day, are now advised. Further studies are needed before final conclusions can be drawn.

Once hemorrhages and exudates appear, the patient can only look forward to their increase since there is no effective therapy. Some of the reports in the literature claiming improvement with various types of therapy must be questioned. Old hemorrhages are constantly being absorbed, while new ones develop. If large hemorrhages are absorbed at a time when the new bleeding is scanty, there may be an appearance of improvement which is only an illusion, since larger hemorrhages usually follow at a later period.

One of the worst features is, however, invasion of the macula which causes a loss of central vision. Fortunately, this is a late development, and not too frequent, for the hemorrhages and exudates tend to surround but spare the macula for a long time.

Vascular changes. An early sign in many cases of diabetes is engorgement and increased tortuosity of the veins. Such changes were reported by Agatston[10] and have recently been studied by Ballantyne and Loewenstein.[8] Pathologic examination shows in many cases a process of phlebosclerosis due to endothelial proliferation which blocks the lumen. Complete blocking of a vein seems to be exceptional, as some canalization is usually found.

The capillaries show a number of changes. Especially near the macula, it is common to

find in the diabetic retina an increased number of capillaries as well as dilatation of their lumens. The hemorrhages probably originate from diseased capillaries which permit the escape of blood through their walls. Some of the diseased capillaries dilate to form micro-aneurysms. The phlebosclerosis causes a blocking of the circulation on the venous side that raises capillary pressure and probably is a factor in producing capillary aneurysms and hemorrhages. Closure of capillary aneurysms by endothelial proliferation was found in a few instances.

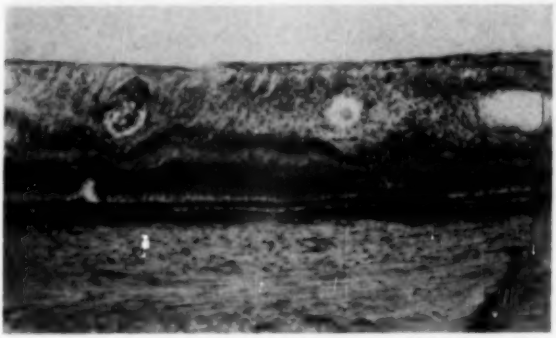

Fig. 7 (Gartner). On the right side is a thick-walled hyalinized arteriole. On the left is a partially occluded vein.

Of the 110 eyes I examined, the youngest patient represented was aged 28 years, but most of the patients were over 50 years of age. They all had had diabetes for a long time. The role of arteriosclerosis was difficult to evaluate, since all of the eyes showed sclerosis in the retinal vessels.

Diabetes accelerates the degenerative changes in the blood vessels and causes premature arteriosclerosis all over the body with a noteworthy increase of its incidence even in youth. Since most diabetics are in the older age group it is even more pronounced in them. Palmer[11] noted a similar increase in the incidence of hypertension among the diabetics.

In the early stages of diabetes, retinal hemorrhages and capillary aneurysms may be seen and even exudates are found before there is ophthalmoscopic evidence of arteriosclerosis. That does not rule out the presence of arteriosclerosis, which can only be done by histologic study. More studies are needed of the eyes in early stages of diabetic retinopathy. The eyes I examined all showed some degree of retinal and choroidal arteriosclerosis along with the diabetic retinopathy.

In the arteries, veins, as well as in the capillaries there were frequently seen irregularities of caliber due to endothelial proliferation. Complete occlusion was not usually found, but canalization of the channel was an interesting feature in all the vessels. This permitted the maintenance of a limited amount of circulation. The partial blocking without complete closure may be a factor in the tendency to new vessel formation in the retina as well as elsewhere in the diabetic eye. The circulation may be sufficient to prevent the extensive hemorrhages noted with rapid and complete venous occlusion in the arteriosclerotic.

New vessel formation in a number of places in the eye is very characteristic of diabetes. Around the area of the disc they are common. Bands of retinitis proliferans in the vitreous usually carry new blood vessels. These vessels are of capillary size or larger, with thin walls of the capillary type.

The common location of the hemorrhages and exudates indicates a common cause. The work of Ballantyne and Loewenstein[5] and others suggests that impaired venous circulation is at fault but that is not proven.

There are changes in the capillaries and arteries as well; their roles need to be evaluated.

The retinopathy due to diabetes may be seen for a long time as it slowly and inexorably progresses while the patient is under insulin treatment and survives many years. The retinopathy of hypertension and arteriosclerosis, on the other hand, carries a much less favorable prognosis, usually indicating a short life expectancy. This is further proof that diabetic retinopathy is not the same as arteriosclerotic retinopathy.

Retinitis proliferans

Large hemorrhages in the retina may burst into the vitreous from which absorption is typically slow. With recurring and large hemorrhages, a point is reached beyond the capacity of the eye to absorb. The blood undergoes degenerative changes and is replaced by connective-tissue bands which are irregularly placed in the vitreous and

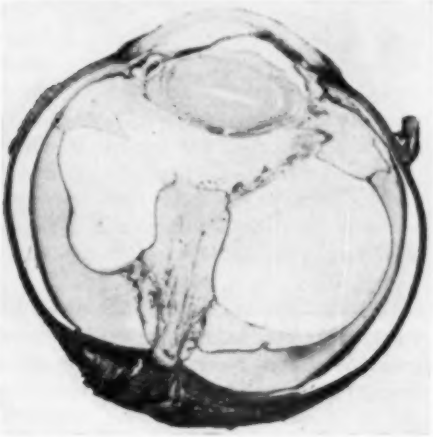

Fig. 8 (Gartner). Retinitis proliferans.

attached to the retina, a condition called retinitis proliferans.

A feature of new connective tissue is its shrinkage during the first period after its formation. As the bands shrink they pull the lightly attached retina away from the

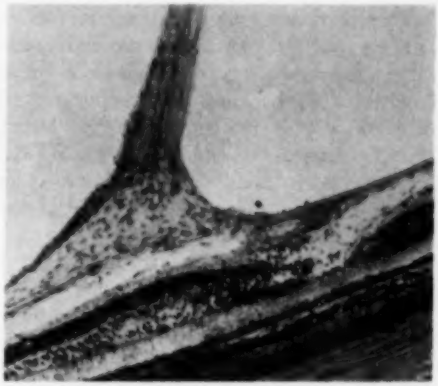

Fig. 9 (Gartner). Retinitis proliferans.

pigment epithelium and cause a malignant form of retinal detachment. This is not amenable to surgery and causes an incurable blindness.

Another type of retinitis proliferans has been described by Klien[12] and Ballantyne and Loewenstein[8] which is predominantly due to the growth of new vessels from the disc or retina into the vitreous. This is supported by a minimal amount of delicate connective tissue. It seems to follow varying degrees of venous occlusion in the retinal vessels. It may also be a reaction to unabsorbed hemorrhage in the vitreous. A similar type of new vessel formation is common on the disc after obstruction of the central retinal vein.

Retinitis proliferans is found in adults, usually over the age of 35 years, and I have not seen it in children. This is probably due to the better circulation in early life. In older people, there are additional factors that impair the circulation.

Lipemia retinalis

Lipemia retinalis is extremely rare, but is briefly mentioned. Koch and Strong[13] reported a case in 1946 and noted that it was the 66th case to be reported; three of these cases unquestionably occurred in patients without diabetes. Lipemia retinalis occurs

with remarkably high blood sugars (above 500 mg. per 100 cc.). It was more frequent in the pre-insulin era. The high blood sugar creates a disturbance of fat metabolism causing a high fat content of the blood, which turns a creamy white color. The retinal vessels stand out as creamy white against a pale retina. With modern treatment, recovery may occur.

Optic atrophy

Optic atrophy of the postneuritic variety or of the type following retrobulbar neuritis has been described. According to Woods this is due to vitamin-B deficiency, especially thiamine chloride, and is aided by vitamin therapy. My own impression is that diabetes is not a frequent cause of optic atrophy.

Changes in the lens

The lens is susceptible to many changes in diabetes. The aqueous which surrounds the lens contains glucose, in proportion to the blood sugar. The lens takes up this glucose, but has a considerable lag in its absorption and later in its discharge.

Refractive errors. With rapid and large blood-sugar fluctuations, refractive changes occur which are best explained by the varied sugar content of the lens with a modification in its osmotic power and water content. This causes a change in the index of refraction and curvature of the lens with rapid increase toward myopia as the usual result. This is transitory and, as Bellows[14] reports, it is always followed by transitory hyperopia before returning to normal.

Transitory hyperopia alone is a rare result of large blood-sugar fluctuations. It seems to appear when the blood sugar diminishes. The temporary myopia and hyperopia when once established require a few weeks to disappear, as this interval is required for the lens to reëstablish its equilibrium. The amount of refractive change to hyperopia or myopia varies, but rarely exceeds 2 or 3 diopters.

Impaired accommodation and precocious presbyopia are occasionally noted in diabetes. This is easiest to detect in patients whose age is under 40 years, and more so under the age of 30 years. With an improvement in the diabetes, there may be partial or complete return of normal accommodation. The site of action of this defect is not clear. While it may be in the lens, there is a possibility that it is due to changes in the ciliary muscle, or in its nerve supply.

Sudden changes in refraction or accommodation should arouse the suspicion of diabetes and appropriate tests should be made to establish the diagnosis.

Cataract in the diabetic is usually of the ordinary senile type and is noteworthy because of its greater frequency, the earlier age at which it appears, and the complications of its extraction.

True diabetic cataract is very rare and can only be defined in those under the age of 35 years. Diabetic cataracts are usually bilateral and start as subcapsular snowflake opacities which progress slowly in most cases. A rare type occurs in young diabetics who suffer sudden and large rises in blood sugar with the development of a cataract which progresses to full maturity in a few days. Once a cataract is mature, it cannot be differentiated from the senile variety. In exceptional cases in young diabetics, a reversal of early lens changes has been reported when the diabetes was brought under control.

Diabetes does not contraindicate cataract surgery, but does indicate the need for more precautions and forecasts more complications. The preliminary tests for light projection should be carefully done, since the cataract may hide extensive retinopathy or retinitis proliferans which would make the best operation of no value. The incidence of postoperative infection is greater in the diabetic, hence exceptional precautions are needed.

Hemorrhage at operation and later is a disturbing feature. The tendency to bleed seems to be increased by rapid changes in

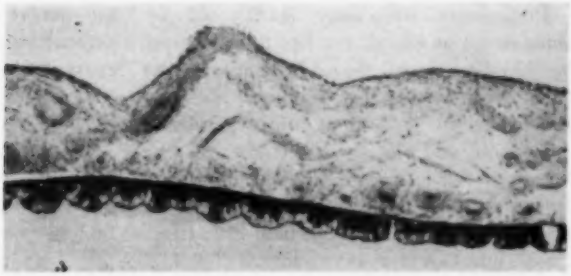

Fig. 10 (Gartner). Diabetic iridopathy.

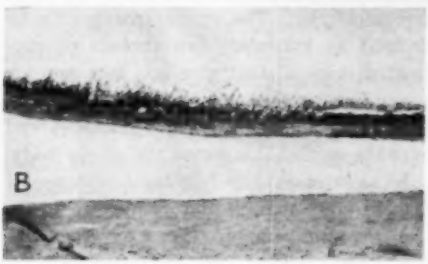

Fig. 11 (Gartner). (A) Cystic degeneration of pigment epithelium in ciliary body. (B) Cystic degeneration of pigment epithelium of pars plana of ciliary body.

the blood sugar and the use of insulin. It is therefore best not to make drastic changes in the control of diabetes just before the patient is going to be operated upon.

Preliminary iridectomy is favored by some surgeons who do not like to be plagued by bleeding from the iridectomy at the time of a combined extraction. My own practice is to proceed as for a combined extraction and do an iridectomy. If the bleeding is excessive, I stop and do the extraction at a later date. If not, the operation is completed with an immediate extraction. Since intracapsular extraction is followed by the least reaction it is the most desirable procedure in the diabetic, and it gives the best optical results. Following extracapsular extraction, a diabetic is much more likely to have considerable reaction and a secondary membrane.

Postoperative hemorrhage occurs with greater frequency in the diabetic. According to the study of Owens and Hughes[15] the level of blood sugar does not have as important an effect as the duration of the diabetes. They reported that, in the group of patients with diabetes for less than nine years, there was an incidence of postoperative hemorrhage of 1.8 percent, while those with a duration of more than nine years had an incidence of 10.4 percent. These figures are similar to those for the occurrence of diabetic retinopathy and suggest a common cause in the vascular damage.

Changes in the Iris

It was noted long ago that, with iris surgery in the diabetic, pigment dispersion often took place as the iris was handled, so that the aqueous turned a cloudy brown. The pathology of the diabetic iris was studied by Becker[16] (1885) and Kamocki[17] (1887-1889) and later by many others. The iris stroma is normal, or in rare cases has some atrophy. The pigment epithelium becomes irregularly swollen and cystic, with some depigmentation. The cystic spaces may be bridged by extremely fine threads of pigmented material that give it a lacy appearance. The contents of the cysts have not been analyzed. In rare cases, cysts extend over the epithelial layer of the ciliary body.

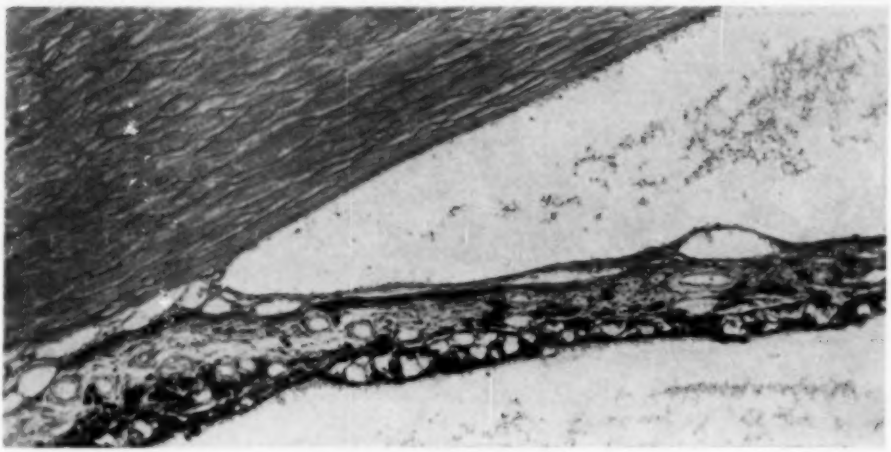

Fig. 12 (Gartner). Rubeosis iridis and diabetic iridopathy.

In most cases with histologic evidence of diabetic retinopathy, the characteristic iridopathy was found. The exceptions are few. The finding of characteristic iris changes can be used as the most reliable diagnostic sign of diabetes. Some semblance of

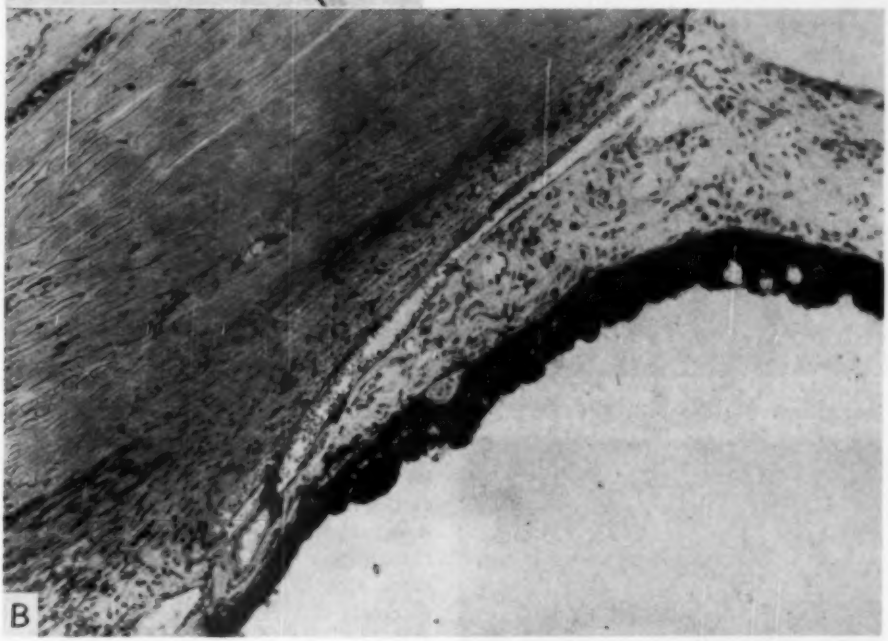

Fig. 13 (Gartner). Rubeosis iridis diabetica. (A) Low-power view. (B) High-power view. This demonstrates the connection of the vessels on the anterior iris surface with the vessels of the ciliary body.

the changes has been very rarely noted in other degenerative conditions but the degree found in diabetes has never been reached. Iritis is believed to be more common in diabetics.

Rubeosis iridis is a complication of diabetes in which the anterior surface of the iris is covered by a delicate layer of connective tissue supporting a network of thin-walled blood vessels. Peripheral anterior synechias form and an intractable glaucoma follows. This was first described by Salus,[18] in 1928. The newly formed vessels on the iris have very thin walls of the capillary type which can be traced toward the angle.

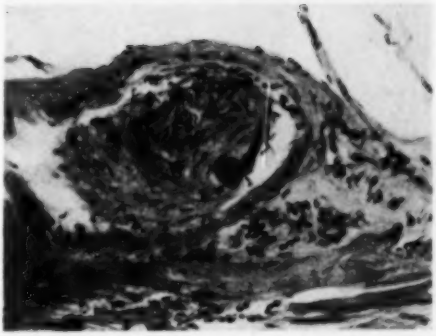

Fig. 14 (Gartner). Partially occluded central retinal artery on the nervehead in a case of rubeosis iridis.

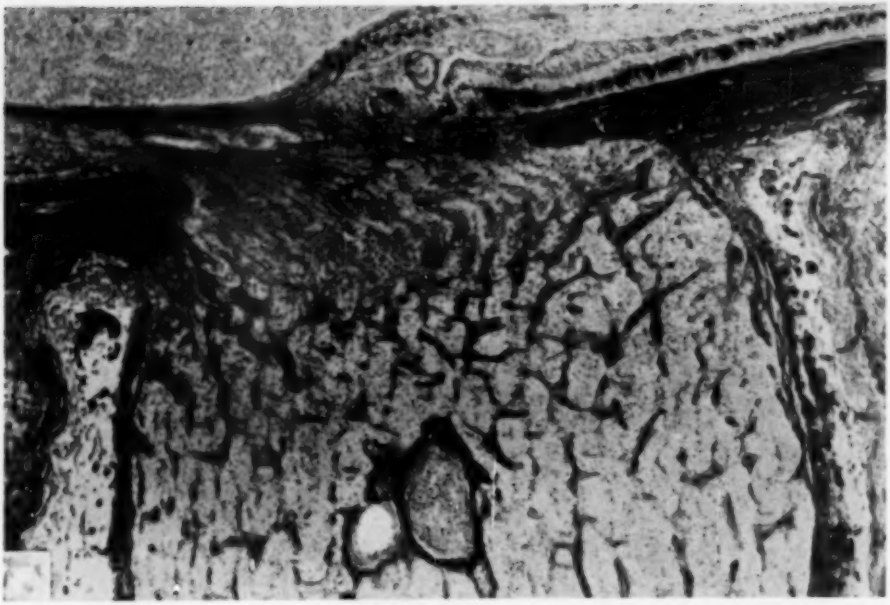

Fig. 15 (Gartner). Occlusion with some canalization of central retinal vein in the optic nerve.

Fig. 16 (Gartner). A high-power view of portion of Figure 15.

These delicate vessels bleed easily and often do so spontaneously. Surgery that involves cutting into the eye causes bleeding from them and only compounds the damage. Cyclodiathermy may relieve some of these cases. Most of these patients have a painful glaucoma that resists medical and surgical treatment and usually require enucleation.

The incidence of rubeosis iridis in the diabetic population is low. However, in the study of 75 cases of diabetes at the Army Institute of Pathology, over three fourths had rubeosis iridis. Most of the eyes studied had, however, been enucleated because of glaucoma. In my collection at Montefiore Hospital of eyes that had been removed at autopsy, no case of rubeosis iridis was found.

Kurz[19] claimed that the newly formed vessels on the iris connected with the canal of Schlemm. These vessels are difficult to trace, especially in the zone of anterior synechias

where they are usually flattened out. I found no connections with the normal iris vessels and none to the canal of Schlemm. Connections were, however, traced to the vessels in the ciliary body.

In a number of eyes with rubeosis iridis, I found almost complete obstruction of the central retinal vein by endothelial proliferation which was canalized, and in a few eyes, partial obstruction of the artery by a similar process. Our sections do not include much of the optic nerve, consequently an extensive pathologic change can be missed if it occurs in the central vessels far behind the globe. Incomplete obstruction of the central retinal vein develops slowly and is accompanied by few retinal hemorrhages in contrast to the extensive hemorrhages typically found in sudden and complete obstruction of the central retinal vein.

The iris picture in rubeosis iridis in the diabetic resembles the description by Samuels[20] of the changes in the anterior part of the eye in obstruction of the central retinal vein. He described new vessel formation on the iris surface, peripheral anterior synechias, a great tendency to bleed and an intractable glaucoma.

A similar mechanism may explain both types of vascular disturbance. The only variation is that, in the diabetic, the slow and incomplete vascular occlusions do not cause extensive retinal hemorrhages. However, the circulation in both types is so impaired that it causes new vessel formation on the iris, peripheral anterior synechias, and a similar malignant glaucoma.

Another possibility is that the development of the newly formed vessels on the iris may be caused by a mechanism similar to that producing the new-vessel formation in the retina and vitreous of the diabetic. The slow venous obstruction noted in the retina may have a parallel in the anterior part of the eye and stimulate new-vessel formation on the iris.

Other ocular changes

Marked ocular hypotony is a diagnostic feature in diabetic coma. It is probably due to a combination of osmotic and toxic factors.

Muscles. Paralysis of the external rectus muscle is not an uncommon finding in diabetes. This is probably due to a neuritis. Palsy of the other extraocular muscles is less common but had been reported. Collier[21] noted the paralysis of the oculomotor nerve trunk, and Hilgartner[22] reported the paralysis of the superior rectus and inferior oblique from diabetes. Recovery from these palsies is usually spontaneous, although a few cases show permanent defects.

Summary

Diabetes is an important cause of visual impairment and blindness. The survival of more old people has increased the numbers suffering from this disease and insulin has prolonged their lives, so that we now see many more patients with diabetic eye lesions. The incidence of diabetic retinopathy increases with the duration and severity of the disease. The best modern care with diet and insulin does not prevent its onset and extension.

The ocular pathology of diabetes was studied in 110 eyes, 10 of which were obtained at autopsy. The others were enucleated during life.

The pathology of diabetic retinopathy is described. There are hemorrhages and exudates associated with extensive vascular damage. The characteristics that differentiate the diabetic from other types of retinopathy are considered.

All the cases showed some sclerosis of the arteries. Endothelial proliferation with canalization was found in many arteries and veins. Disease of the capillaries was manifested by their increase in number, their widened lumens, and the formation of capillary aneurysms, some of which became oc-

cluded by endothelial proliferation.

The iridopathy of diabetes is almost specific for this disease and is of diagnostic importance. Rubeosis iridis may follow slow vascular occlusion by sclerosis and is probably secondary to the impaired ocular circulation.

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Ophthalmic Miniature

The ophthalmic writings of Galen (born 131 A.D.) have been lost. He himself speaks in his extant writings of three ophthalmic treatises that he had written but he speaks of them somewhat slightingly as "a little booklet." One part dealt with optics and another with the diagnosis of diseases of the eye.

Hirschberg, *Graefe-Saemisch, Handbuch.*

AN ATTEMPT TO INFLUENCE CORNEAL WOUND HEALING BY LOCAL APPLICATION OF CERTAIN AMINO ACIDS*

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The attempt to influence wound healing is one of the oldest biologic and medical endeavors. Although the cornea is one of the most suitable organs for studying problems of regeneration, the literature on corneal wound healing is relatively scarce. Since it is on the body surface, the cornea is readily accessible. It is sharply circumscribed and has a certain anatomic independence from the surrounding tissues. Its structural peculiarities, however, necessitate special considerations in any experimental approach.

The cornea has no blood vessels, its respiration and its nutrition are maintained by diffusion from the pericorneal capillaries through the entire substance. The aqueous has a part in its nutrition and, in its respiration, the atmospheric air has some, though certainly a limited, role.

Any injury which interferes with diffusion in the cornea may lead to vascularization and to replacement of lost substance with architecturally inadequate tissue (loss of transparency), two dreaded complications of corneal injuries. In treating corneal wounds, the avoidance of these complications is a prime objective.

How nutritional need affects vascularization of the cornea can be seen clearly from the fact that inadequate diets of different composition produce corneal vascularization. The formation of new blood vessels was observed in protein deprivation and deficiencies of lysine, tryptophan, methionine, leucine, histidine, phenylalanine, threonine, valine, or arginine.

In our experiments (Schaeffer and Geiger) with delayed supplementation of tryptophan, we have shown that, in lack of an essential amino acid, the protein synthesis is disturbed and corneal vascularization and cataract formation are local responses to the nutritional need.

A delayed supplementation of the missing essential amino acid (tryptophan) cannot inhibit corneal vascularization and cataract formation, as the amino acids are not stored in the body and the protein synthesis can proceed only when all essential amino acids are simultaneously present in the tissues. A general and a local starvation of the tissues equally effects vascularization of the cornea.

The present study is an attempt to find an adequate physiologic way of furnishing artificially the nutritional needs of the corneal cells, thus preventing chemotactic attraction of blood vessels and facilitating physiologic regeneration; that is, a restitutio ad integrum of the damaged corneal tissues.

WORK ON TISSUE CULTURES

My previous experimental work on tissue cultures suggested a certain similarity of the living conditions of explanted cells and those of the cell elements of the damaged cornea. This similarity is based mainly on the fact that the blood supply is missing in both and, therefore, the nutrition of the cell units is effected by a somewhat different mechanism from other parts of the organism.

The cells of the tissue culture have to be fed with substances which can be directly assimilated by the cells without participation of an intestinal tract and a liver. This food material must contain all the necessary building elements of the protoplasm, or at least their precursors from which the cell is able to synthesize the components of growth. It is logical to assume that the corneal cells can be nourished in a similar way when the normal nutritive exchange of the cornea is handicapped by injury.

In previous investigations, I attempted to

* Read before the Los Angeles Ophthalmological Society, February, 1949.

influence regeneration of the corneal epithelium and healing of deep corneal wounds with local application of embryonic tissue extract, the so-called trephones, with very promising results. These substances were described as follows: "The tissues of mammalian or avian embryos contain principles

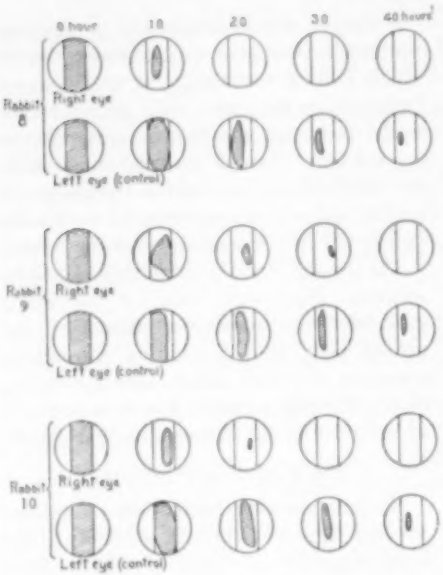

Fig. 1 (Schaeffer). *Healing of experimental epithelial erosions in guinea pigs.* Recordings on three animals. Right eye treated with standard amino-acid mixture; left eye with physiologic saline solution.

from which fibroblasts (in vitro) are able to synthesize protoplasmatic building stones. In this way an unlimited proliferation of the culture is made possible. Carrel called these principles 'trephones,' from the Greek, τρεφω, (nourish). Their action is not only like that of hormones or enzymes, but they represent true assimilable nutritive substances, which when added to neutral cultural media, such as fibrin suspension and salt solution, warrant unlimited growth."

The clinical application of trephones has been hampered, however, mainly by their extreme lability. At room temperature, they lose their activity with a simultaneous dropping of pH. At a temperature of 38°C., they are not completely destroyed in 48 hours. Their practical use is hindered also by the fact that they become readily contaminated.

Of course, the trephones are not well-defined substances and, therefore, can not be substituted readily by chemically well-defined substances, although attempts in that direction, even with partial success, have been made. In recent experiments, Fischer succeeded in maintaining live tissue cultures in a medium in which all components were chemically well known. He frequently made the observation that, in the otherwise inadequate culture medium, the dying cells suddenly began to proliferate. This unexpected growth was partly due to autolysis of parts of the tissue and partly to digestion of the protoplasma coagulum. Obviously the products of this protein decomposition were used to maintain and prolong life in the dying culture. This observation led to the finding that certain amino acids in these inadequate media have a catalytic effect on growth.

Methods

First experiment

Encouraged by Fischer's results, an attempt was made to influence the regeneration of experimental wounds of the cornea by local administration of amino acids in vivo. The technique employed was a modification of the method of Gundersen and Liebman.

Superficial vertical incisions were made across the corneas of guinea pigs into the epithelium of both eyes by means of a double knife with blades two mm. apart. The cornea was immediately stained with fluorescein and the epithelium between the two lines evenly abraded with a spatula. The epithelium in this area has to be cleaned off completely, otherwise remaining cell islands shorten the healing period.

The corneas were periodically stained and the fluorescein-positive areas registered on a chart drawn on graph paper. The chart con-

sisted of a ring symbolizing the limbus with a vertical double line in the center. By counting the number of stained and unstained squares on the paper, a quantitative expression of the healing process could be obtained. The biomicroscopic examination of this process is indispensable. Complete healing was registered when no lesions or irregularities of the corneal surface could be registered.

The amino-acid solution was made in 0.6-percent saline solution. It contained 2 mg. of cystine, 5 mg. of proline, 6 mg. of asparagine, and 14 mg. of glutamine per ml., and was adjusted to pH 7.2. The ointment was prepared by emulsifying 70 mg. of aquafor with 30 ml. amino-acid solution which contained the aforementioned amino acids in 10-fold concentration.*

In 18 of these animals the amino-acid solution was dropped into the right eye every hour while the left (control) eye received a corresponding amount of physiologic saline solution. In the remaining 18 animals an ointment containing the amino acids was applied twice a day to the right eye together with a five-percent boric-acid ophthalmic ointment which was applied to both eyes.

Second experiment

The same experiment was repeated on six other animals, but instead of a stripe, a round erosion, 3.5 mm. in diameter, was made in a similar manner with a trephine.

Results. A complete regeneration of the corneal defect in the eyes treated with amino acids was achieved within 12 to 42 hours (average, less than 30 hours), while the healing process in the control eyes required from 55 to as long as 120 hours.

Third experiment

In a third series of experiments the effect of amino acids on healing of deep non-perforating trephine wounds of the cornea was examined. In 12 rabbits a central defect, 2.5 mm. in diameter and 0.4 mm. deep, was made into the substance of the cornea of both eyes. The right eye was treated in two animals with hourly administration of drops containing amino acids while the left eye received saline solution. The other animals received ointment applications as in the first experiment.

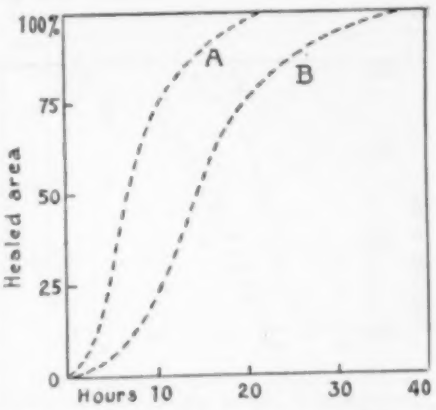

Fig. 2 (Schaeffer). *Healing of experimental corneal erosions.* (A) Treated with standard amino-acid mixture. (B) Not treated.

In the eyes treated with amino acids, the corneal defect was covered with epithelium within 32 to 56 hours and in the control eyes between the 4th and 5th day. The biomicroscopic parallel with the histologic examination showed that in the eyes treated with amino acids the same phase of the healing process is reached after two days which the control eyes attain only after the sixth day of experiment.

Second series of investigations

In a second series of experiments this investigation was repeated, with more rigid routine and under better standardized external conditions. Weight of the animals, food, and room temperature were kept uniform.

Before operation the eyes were washed

*I am indebted to Dr. E. Geiger, professor of pharmacology, University of Southern California, and to Mr. J. D. Murray, chemist, H & M Laboratories, Los Angeles, for help in making the solutions and in estimating the osmotic pressures.

with penicillin in saline solution. Under such conditions 24 guinea pigs were treated as in the preliminary investigation, using only vertical stripe-shaped corneal erosions as the testing method—the ring-shaped erosion did not represent any advantage and was harder to do with the same exactness as the stripe-shaped erosion.

The healing process was registered as in the first series of investigations with the addition that, from the obtained data, the middle values were recorded on a coördinate system obtaining a curve of the healing process.

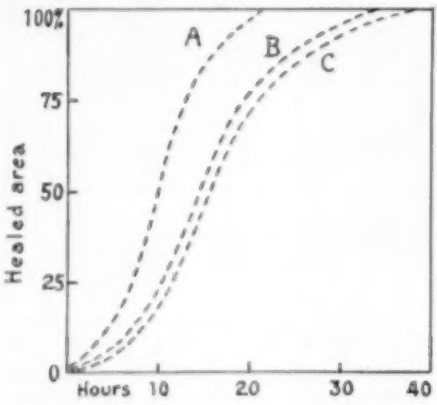

Fig. 3 (Schaeffer). *Healing of experimental corneal erosions.* (A) Treated with standard amino-acid mixture. (B) Treated with amino-acid mixture in which cystine is substituted by methionine. (C) Treated with amino-acid mixture containing neither cystine nor methionine.

Results. In this second series of experiments, the recorded data became more uniform and the healing period, especially for the control eyes, became somewhat shortened.

While the healing of the epithelial wound was accomplished in an average 36 hours (36 to 48 hours) in the control eyes the amino-acid treated eyes healed in slightly less than 20 hours (12 to 29 hours). No considerable difference was registered between drops and ointments. In this series of experiments the drops were administered every half hour.

Mode of action

An explanation of the proliferation-stimulating activity of these amino-acid mixtures presents something of a problem. It can be assumed that the amino acids were partly assimilated by the proliferating cells and were used as building stones for new protein, although alone they are quite inadequate for protein synthesis.

The role of sulfhydryl radicals (-SH) in tissue growth has been shown by Hammett. Many different preparations containing this group have been used in an attempt to influence wound healing. The biochemist, Elvehjem, expressed the belief that glutathione and other substances containing -SH have a direct biologic relation to growth. The mechanism by which this radical is used is, of course, not well understood, but it is likely that its effect is due to indirect activation of various enzymes for growth and respiration.

Thus it is highly probable, as already assumed by Fischer, that, in this amino-acid mixture, the activity was mainly due to the presence of cystine, an S-containing amino acid, which he found to activate proliferation in vitro. This is, of course, very surprising for in the organism methionine is the essential S-containing amino acid; for the in vitro cell elements this was found not to be the case.

In vitro, the cells are unable to perform the demethylation of methionine and to build cystine. Thus cystine becomes essential. To explain the extraordinary importance of cystine in improving the otherwise unappropriate culture media, one is reminded of the fact that many enzymatic systems are activated by the thiol group, like glutathione, and it may be that binding heavy metals to the -SH also has a part.

The activation of proteolytic enzymes by -SH has been shown in many fields of the chemical research (Karrer, v. Euler, Hop-

kins). The role of cystine in activation of inadequate culture media might be of this order. Cystine is a disulfide which, in combination with the sulfhydryl of the cells, maintains a dynamic balance of -SS- -SH. Our findings can be summarized with the statement that cystine might function in the in vitro culture media, as well as on the damaged epithelial surface of the cornea, both as an energy-furnishing ingredient and as a growth catalyst. It apparently plays a major role in the maintenance of life in inadequate cultures and in the acceleration of healing of a corneal wound.

To prove our contention we repeated our experiments in two different groups of animals, using the modalities of the first experiment; in one series, cystine was completely eliminated from the amino-acid mixture, and in the other, cystine was replaced by DL-methionine. The mixture contained two mg. DL-methionine to the same proportional content of the other amino acids as cystine in the original cystine-containing mixture.

In a series of six animals a mixture containing four mg. methionine was also tried, to forestall the objection that, from the DL-methionine, only the natural part would be utilized and thus a two mg. methionine content could not replace the two mg. of cystine. However, no special difference could be detected if one or the other quantity was represented in the mixture.

Results. The curves of the healing process revealed the following data:

1. The amino-acid mixture without cystine has very little or no effect on the speed of epithelization.

2. The slight stimulating effect of the mixture containing methionine instead of cystine is considerably lower than that of cystine-containing mixtures.

The apparent, though low, activity of the methionine mixture might be explained by the fact that in experimental corneal wound-healing processes, the conditions are not equal to those in tissue cultures. Factors of proliferation are also furnished through endogenous ways which might find utilization for methionine. The experimental conditions seem to be a mixture of those found in vivo and in vitro.

Effect of pH and osmotic pressure

Another question of importance concerning these experiments was the maintenance

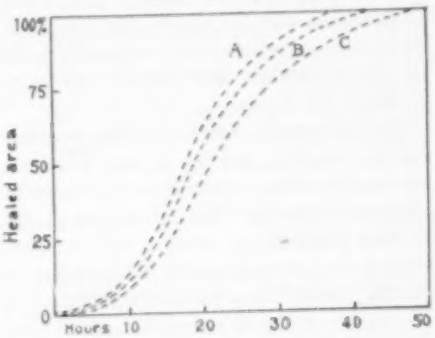

Fig. 4 (Schaeffer). *Effect of tonicity of sodium-chloride solutions on the healing of experimental corneal erosions.* (A) Varying concentrations from 0.8-percent to 1.4-percent sodium-chloride solutions. (B) 0.7- or 1.5-percent sodium-chloride solution. (C) 0.6- or 1.6-percent sodium-chloride solution.

of adequate pH and osmotic pressure in the fluids used in medication. Of course, a buffering of the mixture is required but, since amino acids are amphoteric substances, they keep their pH longer. An adequate pH is estimated to be around 7.2, although the cornea tolerates variations between 6.4 and 8.4 without discomfort.

A more important problem to be solved in our experiments is the maintenance of an adequate osmotic pressure of the applied fluids. The importance given to the osmotic pressure is based on the supposition that tears have an osmotic concentration similar to that of a 1.4-percent NaCl solution. In 1889, Massart calculated the tonicity of the tears, though he accomplished his calculation in a very inadequate way—in two human subjects, drops of different osmotic pressures were instilled over the eyeball (in the

nasal corner) and the isotonicity was estimated from the sensation produced. Massart concluded that 1.39-percent NaCl solution is isosmotic with tears.

These findings were generally accepted and, in the latest ophthalmic literature (collected in my monograph "Ophthalmo-Pharmacology") special emphasis is given to the necessity of improving the adequacy of collyria by adjusting their osmotic pressure to an isosmosis with 1.4-percent NaCl solution. Such recommendation was repeatedly given by Elvin, Mellen and Seltzer, Arrigoni, Fischer, and Tozer.

The adjustment of the osmotic pressure can be accomplished by adding a certain amount of sodium chloride to the otherwise complete collyrium. The calculation of the amount necessary to render a collyrium isotonic is in accordance with the formulas of Nicola, serving as a basis of calculation in the papers of the above-mentioned authors. In all these calculations, the isotonicity of tears with a 1.4-percent NaCl solution is taken for granted.

A recent paper of Krogh, Lund, and Pedersen-Bjergaard brought a new light to these problems, which will necessarily modify our conception in regard to the tonicity of tears. These authors collected lacrimal fluid from the lower conjunctival sac of a small number of persons and the concentration of these fluids was estimated by the very accurate vapor-pressure method, first proposed by Hill and modified by Krogh.

They found that the tear fluid (an average of the individuals tested) was isosmotic with a 0.9-percent NaCl solution, the concentration varying between 0.87 and 0.92 percent; while the osmotic pressure of the serum of these same individuals was found to be, on an average, 0.86 percent. Of course, the possibility of slight condensation of the lacrimal fluid by evaporation could not be excluded. Thus, the lacrimal fluid may be considered to be "physiologic" in regard to osmotic concentration, being roughly isosmotic with a 0.9-percent NaCl solution.

These same authors also repeated the investigations of Massart, in which the sensitivity of the eye was tested against different concentrations. They found that the average "untrained" eye cannot distinguish variations between 0.6 and 2.0-percent osmotic equivalents, while a "trained" subject found a 1.5-percent concentration disagreeable.

Considering these contradictory data, I investigated the influence of variations of osmotic concentration on the healing of the corneal wounds previously described, using NaCl solution in concentrations of 0.6, 0.7, 0.8, 0.9, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, and 1.6 percent. The right eye was treated with the standard amino-acid solution adjusted to isosmosis with the NaCl solution used for the left eye. In all cases the same experimental technique of the two mm. vertical erosion of the corneal epithelium was applied. Each osmotic concentration was tested on six animals.

The results were registered as a curve of epithelization and they can easily be summarized as follows:

1. Salt concentrations of 0.9 to 1.3 percent do not influence the rate of epithelization in any way.

2. Concentrations lower or higher than these two values begin to inhibit the healing process, though at 0.8 or 1.4 percent no definite inhibition can be registered. Slight inhibition becomes noticeable at values of 1.5 or 0.7 percent concentrations. At concentrations of 0.6 or 1.6 percent respectively, the inhibition is definite.

3. The inhibitory effect of hypo- or hypertonicity in the amino-acid solution is independent of the stimulating effect of the amino acids themselves. The rate of epithelization shows inhibition at similar grades of hypo- or hypertonicity, as in the NaCl solutions, though this inhibitory effect is somewhat slighter than in the case of NaCl solutions.

The effect of tonicity was also tested subjectively on 12 untrained normal individuals. I, myself, was not able to distinguish con-

centrations from 0.7 to 1.6-percent saline, although concentrations lower or higher than these variations were received with unpleasant sensations. The discomfort was definitely related to the grade of discrepancy from the so-called physiologic limits. In testing isosmotic buffered amino-acid mixtures instead of NaCl solutions, the resulting sensations were the same. The unpleasant sensation was dependent exclusively on the osmotic concentration of the fluids.

When the same solutions were tested on 12 different individuals with healthy normal eyes, the results were about the same. One person found a 1.8-percent concentration definitely disagreeable; while three subjects began to register a slight unpleasant feeling at 1.7 percent; the rest, at 2.0 percent. On the other hand, a concentration of 0.6-percent solution was distinguished by all except one subject, who was able to distinguish concentrations only under 0.5 percent. No one recognized the difference between hypo- or hypertonicity; the comfort or the discomfort experienced was always unspecified. No difference in sensation was experienced with solutions between a 0.6 and a 1.8 percent.

Clinical trial

The results of the treatment of experimental corneal wounds with amino acids encouraged clinical trial. Since a quantitative evaluation of the therapeutic effect of this treatment is very difficult, if possible at all, an adequate estimate will be possible only after study of a much greater number of cases. It must be emphasized that the amino-acid mixture was never administered alone and, therefore, the rate of healing was the result of different factors, often opposite in their effect. Some local anesthetics and disinfectants inhibit regeneration.

To date 208 cases have had regular follow-up, though all were cases in which healing was expected within one to several days. Although these trials do not furnish quantitative data, the general impression was that the healing period was shorter than ex-

TABLE 1

Type of corneal injury and average healing time in control and amino-acid treated animals

Exper. No.	Experimental Injury	Treatment		No. of Animals	Healing Time*	
		Control	Amino-acid Treated		Control Eye	Treated Eye
Guinea pigs						
1a	Vertical erosion, 2 m.	Physiol. saline hourly	Amino-acid sol. hourly	18	64 (55–108)	22 (15–32)
1b		5% boric acid ointment twice daily	5% boric acid ointment containing amino acids twice daily	18	78 (66–120)	26 (12–42)
2	Round erosion, 3.5 mm.	Physiol. saline hourly	Amino-acid sol. hourly	6	62 (50–112)	21 (14–38)
Rabbits						
3a	Deep non-perforating trephine wound	Physiol. saline	Amino-acid sol. hourly	2	95 (86–104)	35 (28–42)
3b		5% boric acid ointment twice daily	5% boric acid ointment containing amino acids twice daily	10	108 (96–120)	40 (32–56)

* The first figure gives the average value and those in parentheses the minimum and maximum values of the individual experiments.

pected. The rate of healing in cases selected at random, with no similarity in condition or etiology, does not furnish a specific basis of comparison, except on a large statistical scale. The cases treated with amino acids were:

1. Accidental (traumatic) erosions and deep nonperforating wounds of the cornea, 62.

2. Spontaneous erosions, 3.

3. Corneal lesions due to foreign bodies and their extraction, 85.

4. Postoperative lesions of the cornea and conjunctiva, as after resection of pterygium, benign growths (one case of partial keratectomy), 32.

5. Therapeutic lesions in case of herpetic keratitis (for example, destruction of surface epithelium with strong iodine solution), 8.

6. Corneal ulcers due to organisms (one hypopyon ulcer), 12.

7. Keratitis (superficial punctate, sicca, e lagophthalmo), 6.

Comments

There is sufficient evidence that isolated cell units are able to utilize amino acids furnished by exogenous supply and, among the amino acids thus offered, cystine shows a definite function in stimulating proliferation. In local treatment of corneal wound surfaces, cell units also seem to be able to assimilate amino acids administered locally, thus gaining stimulation of the healing process.

The present experiments attempted to evaluate quantitatively the rate of epithelial regeneration and to determine the acceleration in the healing rate due to local administration of amino acids.

The analogy between tissue culture and exposed cell units on wound surfaces, which has been mentioned, is of course, very vague. A tissue culture is an isolated system, in which all external and internal factors of growth can be experimentally controlled. How far the results on tissue culture can be transported by analogy to problems of corneal regeneration remains a problem for further experimentation; however, a certain similarity of the two conditions is undeniable. It is very likely that in both situations cystine accelerates proliferation, though on wound surfaces in vivo the conditions of proliferation are much more complex than in vitro. Furthermore, in addition to the exogenous factors, the endogenous factors of wound healing also play a major role. A tissue culture which is not adequately fed dies within a short time; a corneal wound may heal without addition of any external nutrition. However, the exogenous alimentation of the wound shortens considerably the rate of healing.

Fischer has shown, in feeding isolated tissue fragments in vitro, that cystine has a key position among the amino acids. Cells cannot be kept alive without cystine; the culture dies within 24 hours. The practical application in vivo of substances containing cystine or related compounds for stimulation of wound healing was previously attempted by Hammett. Riley used cystine hydrochloride in the form of a five-percent ointment to favor healing of epithelial skin defects of various kinds. Methionine was also found to have a favorable effect on wound healing if fed to experimental animals. Localio and Morgan found that feeding DL-methionine to protein-depleted rats (150 mg. for 10 days) decreased the consequences of protein depletion.

The assumption that tears are isosmotic with a 1.4-percent sodium-chloride solution can hardly be maintained, since Krogh and others have shown that tears have an osmotic equivalent of physiologic saline solution although the eye is accustomed to tolerating higher osmotic pressures. Our findings confirm Krogh's investigation and add further experimental evidence.

Certain findings of Gundersen and Liebman—that tonicity variations in solutions of anesthetics from the supposed isosmosis of 1.4-percent sodium-chloride solution interferes with epithelization—presented a disturbing alternative. A closer analysis of their

experimental results shows, however, that the difference is more apparent than real.

They found that, in comparison to a 10-percent solution, a four-percent cocaine-hydrochloride solution in distilled water had a much lower inhibitory effect upon epithelization. The same four-percent cocaine-hydrochloride solution in 1.2-percent saline solution—a mixture which according to these authors should be roughly isotonic with tears—is almost completely noninhibitory. On the other hand, a one-percent phenacaine-hydrochloride or a 0.5-percent tetracaine-hydrochloride solution had a negligibly low toxic effect, as did 0.5-percent tetracaine hydrochloride in a five-percent saline solution.

If the osmotic equivalents of these solutions are estimated, we find a very peculiar situation. Considering the fact that the molecular weight of cocaine hydrochloride is 303.17; phenacaine hydrochloride, 352.67; and tetracaine hydrochloride, 300.68, evidently the lowest osmotic equivalent is possessed by the 0.5-percent tetracaine hydrochloride which has one of the lowest inhibitory effects on epithelial regeneration, although from the very low osmotic concentration a greater inhibition could be expected.

If in the inhibition the osmotic condition alone, and not also the toxic effect of the local anesthetic, were the dominant inhibitory factor, a 10-percent cocaine-hydrochloride solution should logically be less than half as inhibitory as a four-percent solution, and about 20 times less inhibitory than the tetracaine hydrochloride solution. Just the opposite findings were recorded.

Calculating the osmotic pressure in terms of ionic strength compared to the ionic strength of sodium chloride, we obtained the following values for the solutions used by Gundersen and Liebman:

Solution	Equivalent with Sodium Chloride
4% cocaine	0.687%
10% cocaine	1.715%
1% phenacaine	0.165%
0.5% tetracaine	0.0971%

It is even more difficult to explain the finding of Gundersen and Liebman that 0.5-percent tetracine hydrochloride in a five-percent saline solution also had a low inhibitory effect on epithelization. In our analysis, a slight inhibition was registered at an osmotic concentration of 1.7-percent sodium chloride. A five-percent saline solution alone causes an intense burning sensation in nontraumatized, normal, although not anesthetized, human cornea. According to our findings, a higher grade of inhibition may be expected. However, this expectation has not, as yet, been verified by experimentation.

Our findings necessitate the modification of the concept of the osmotic concentration of the lacrimal fluid, especially because of the generally accepted recommendation for adjusting the osmotic concentration of collyria to the presumed isosmosis with 1.4-percent sodium chloride.

There is no experimental evidence to support such a recommendation; and there is much more evidence that a lower osmotic concentration, somewhere around 0.9 percent would fit the purpose more adequately.

Summary

1. Local application of certain amino acids accelerate the process of healing of experimental corneal wounds in guinea pigs and of deep nonperforating wounds of rabbit corneas. The epithelization-stimulating effect of the amino-acid combination is due mainly to its cystine content, since without cystine the same combination is devoid of such an effect. Cystine cannot be substituted by methionine, a fact which coincides with findings in tissue cultures in vitro, showing that methionine has no stimulating effect on the proliferation of isolated cell colonies. For the cell units, isolated on the corneal wound-surface by injury, cystine seems to be the essential S-containing amino acid, instead of methionine, just as was found in tissue cultures by Fischer. Methionine in the amino-acid combination has very little or no effect on the rate of epithelization.

2. The amino-acid solutions having an

osmotic concentration equivalent with 0.9-percent to 1.3-percent NaCl solutions are adequate; variations between these two values have roughly the same effect on the rate of healing process. Only osmotic concentrations lower or higher than these values have an inhibitory effect on the regeneration of the damaged epithelium.

The present experiments confirm the conclusion of Krogh and others that tears normally have an osmotic concentration of 0.9-percent NaCl and, therefore, an adjustment of the osmotic pressure of the applied fluid to an isosmosis with 1.4-percent saline is undesirable. This same principle can be extended to all collyria, of which the osmotic concentration might be adjusted to values anywhere between 0.9-percent to 1.3-percent saline solutions.

3. The same amino-acid combination was applied to clinical cases. The results of this investigation are encouraging, although no quantitative evaluation was attempted, because the observations were too limited.

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A CONGENITAL LEVATOR AND EXTERNAL RECTUS MUSCLE INTERNUCLEAR ASSOCIATED REFLEX*

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Each of the cases of a pathologic associated reflex to be presented at this time is a demonstration of a possible internuclear connection between the sixth and third cranial nerve nuclei. In one instance, the association is between the sixth and the third nerve nuclei on the same side; in the other, the association is between the sixth nerve nucleus on one side and the third nerve nucleus upon the opposite side. It is interesting that these also, with some of the other oculomotor associated reflexes, have as the efferent pathway the innervation to the levator palpebrae superioris muscle, and that this efferent pathway is not from or of the autonomic system.

In the first of these two cases, that of a young lady, aged 15 years, also with a bilateral associated jaw-winking reflex (Marcus Gunn phenomenon), there was a congenital paresis of both external rectus muscles: a paresis of the superior rectus muscle in the right eye and a lesser degree paresis of the inferior rectus muscle on the right; in the left eye, there was a partial paresis of the levator, that is, an incomplete ptosis, and a partial paralysis of the superior oblique muscle.

Figure 1 shows the patient in repose; she shows nothing but a bit of ptosis in the left upper lid. Figure 2, showing attempted right lateral rotations, now a demand upon the paretic right external muscle, illustrates an elevation of the ipsilateral upper lid, that is, a contraction of the levator muscle. Figure 3 shows attempted left lateral rotations, and is now a demand upon the left external rectus muscle. With this there occurs an equally sharp elevation of the left upper lid.

Walsh,[1] in analyzing the various types of jaw-winking, called attention to one subdivision of these cases in which contraction of the internal rectus muscle caused a narrowing of the palpebral fissure. In these cases there was also a paralysis of the external rectus muscle. The pathologic association just described is an exact reverse of this.

Fig. 1 (Spaeth). Patient in repose. The bit of ptosis in the left upper lid is evident.

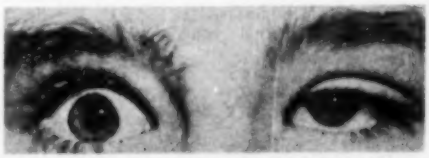

Fig. 2 (Spaeth). Attempted right lateral rotations. This is accompanied by a marked elevation of the right levator muscle.

Fig. 3 (Spaeth). Attempted left lateral rotations. A certain degree of concomitancy is evident. There is a definite, though minimal, amount of left lateral rotation present in each eye, a definite elevation of the left levator muscle accompanies this attempt.

In this instance, there is certainly a pathologic association between the sixth nerve nucleus on each side of the brain stem with

* From the Graduate Hospital of the University of Pennsylvania Graduate School of Medicine. Presented before The Philadelphia College of Physicians, Section on Ophthalmology, January, 1949.

the third nerve nucleus of the same side, as well as, in all probability, with the third nerve upon the opposite side. This case also has, as previously described, an associated jaw-winking reflex. This second pathologic associated reflex is quite relevant to the present subject, although not for the moment.

Fig. 4 (Spaeth). Patient in repose. Slight ptosis, upper lid on left; pupil on left slightly larger than right.

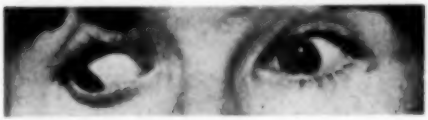

Fig. 5 (Spaeth). Ocular movements down and to the right. Internal rectus muscle and superior oblique muscle limitations on the left. The action of the right external rectus muscle seems to be normal.

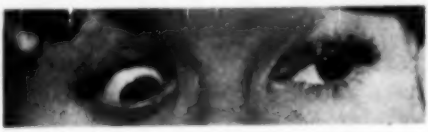

Fig. 6 (Spaeth). Ocular movements down and to the left. By comparison with the right, there is limitation of the left external rectus muscle and of the left inferior rectus muscle.

The second case was that of a young lady who, in repose, demonstrated a slight ptosis of the upper lid on the left. With it, she also had a paresis of the left superior oblique muscle and the left medial and inferior rectus muscles.

Figure 4 shows her condition in repose. She has a slight ptosis of the upper lid, on the left, and a slightly larger pupil on the left as well. Figure 5 illustrates the ocular movements down and to the right; and Figure 6 illustrates the movements down and to the left.

There is a demonstrable external rectus muscle paresis on the left side. There is also, very likely, an internal rectus muscle palsy on the left. Movements in the right eye in the vertical are practically normal. The elevation of the left eyebrow is due to the ptosis.

Figure 7 illustrates some possible left superior rectus muscle limitation. Figures 8 and 9 show some limitation, perhaps, in the action of the left inferior oblique muscle.

The right and left lateral movements were accompanied by a most dramatic demonstration of an external rectus and levator muscle association; in this instance, however, one contralateral from the other.

In Figure 9, movements toward the right are accompanied by a rather sharp elevation of the contralateral, otherwise ptotic, left upper lid, that is, an associated innervation of the left levator muscle.

Figure 10 is even more striking in that the minimal, but definite, amount of ptosis of the upper lid on this side becomes quite evident (see Figure 4), and hence the simultaneous elevation of the right contralateral upper lid is even more striking.

This patient had at various inconstant times a slight dissimilarity in the size of her pupils, the left at times being slightly larger. Figure 4 shows this. Her vision was 6/6 and 6/9. There was no pathologic condition of the fundus. In repose the patient had from 30 to 35 degrees of exophoria. Accommodation near points were normal and equal.

When first seen (four years ago), this young lady of more than average intelligence, was 15 years of age. She was presented for comment by Dr. Lester H. Quinn at the Dallas Medical and Surgical Clinic, in 1945, at Dallas, Texas.

This patient, who did not have a Marcus Gunn phenomenon, demonstrated a third and sixth nucleus internuclear pathologic associated reflex of a crossed type, that is, the external rectus muscle on the one side with the levator muscle on the opposite side.

These cases, at the present time, are under

treatment by muscle surgery to minimize the conspicuousness of their defects. That treatment is not relevant to this presentation; it does, however, emphasize the rather marked cosmetic blemish present in these cases, namely, the unusual appearance of these pathologically associated movements.

Some time ago,[2] I discussed at some length, before this society (The Philadelphia College of Physicians), a consideration of likely, or almost necessary, neuronal intercommunications between the nuclei of the facial, the trigeminal, and the oculomotor nerves in an attempt to explain the pathologic association which exists between the third division of the fifth nerve and nerve supply to the levator of the upper lid (third nerve and/or autonomic) accounting for the Marcus Gunn jaw-winking reflex, or as Wartenberg[3] called it, a pterygoid-levator synkinesis.

A repetition of the reasons presented at that time are not directly relevant to this presentation except that this presentation and the association reflex being presented herein seem to suggest even more than before the possibility of brain-stem internuclear connections as responsible for the associated movements of the Marcus Gunn reflex.

These allied pathologic associated reflexes or associated movements were subjects on which Lutz[4] theorized at great length. A very brief abstract of his opinions is that, in general, "these various pathologic associated reflexes are produced by alterations in the supranuclear connections of the bulbar nuclei; these connections travelling in the posterior longitudinal bundle; . . . the basic pathology being a lesion of the inhibitive mechanism."

The association in Case 1, herein presented, of a Marcus Gunn reflex with an external rectus-levator muscle associated reflex may illustrate this and therefore separate that case from the second presented (that is, these cases may have nothing whatsoever in common). This is improbable, however, for it seems unlikely that alterations in supranuclear connections could cause the isolated paralyses in either of the two cases of associated reflexes herein described, hence a tendency to disagree with Lutz.

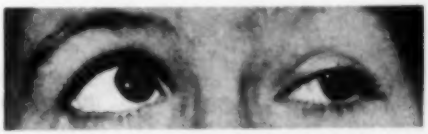

Fig. 7 (Spaeth). Movements up and to the left. The left levator and superior rectus muscles both show limitation in movement. The levator muscle limitation is rather evident.

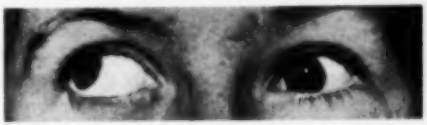

Fig. 8 (Spaeth). Ocular movements up and to the right. Limitation in the movement of the left inferior oblique muscle is evident. The limitation of movement of the left internal rectus muscle is the same as in Figure 5.

Fig. 9 (Spaeth). Right lateral rotations, on the horizontal, result in a sharp elevation of both levator muscles, especially outstanding in the paretic levator muscle on the left.

Fig. 10 (Spaeth). Left-lateral rotations. In this, as would be expected, the contraction of the contralateral right levator muscle is very evident because of the comparison with the left paretic levator muscle.

Wartenberg,[3] has gone into great detail to show that these various associated movements, both the congenital and the acquired

forms, are to be answered upon a basis rather similar to that propounded by Lutz, but his work is much more searching and analytic in nature. He states, that, "all . . . types of associated movements can be regarded as expressions of phylogenetic regression."

Quoting him: "In intrafacial movements it is evident; it is apparent in intraocular associated movements; it is very probable in the winking-jaw phenomenon; (the oculomandibular association); it is very reasonable to assume that the same mechanism of release is at work in the jaw-winking phenomenon of the Marcus Gunn."

It would seem that the first of these four categories mentioned by Wartenberg is quite different from the other three and therefore hardly to be used as a proof of the assumption put forth. The reasons stated for the fourth category are unsatisfactory when one considers meticulously the varied oculomotor findings[8] seen in these cases of the Marcus Gunn associated movements—the paralyses and the apparently unaccountable muscle contractions;[6] the absence of some ocular muscles suggesting a failure of innervation to the periaxial mesoderm during the embryologic formation of the ocular muscles; certain signs pointing to a nuclear source, others suggesting an internuclear origin; generally a complete ocular asymmetry which can hardly be consistent with the contention that these movements are supranuclear in origin and of phylogenetic regression.

There is one more factor which stands out rather clearly throughout this presentation. This is the sharp difference which exists between the sixth cranial nerve and the nucleus of the sixth cranial nerve. The sixth cranial nerve supplies only the ipsilateral external rectus muscle. The sixth cranial nerve nucleus not only supplies, normally, the lateral rectus muscle of the same side but, in addition, it *is connected with* the innervation to the superior rectus muscle, the medial rectus muscle, and the inferior rectus muscle—all of the contralateral side.

These fibers apparently pass to the third nerve nucleus of the same side by way of the medial longitudinal bundle; they may represent collaterals of the sixth nerve fibers in their intramedullary course or fibers of an internuncial system.

In any case, they seem to split up around the cells of the ipsilateral third nerve nucleus according to Bing[7] and others (Lewy, F. H.).[8] From here, third nerve fibers cross the midline and leave the brain stem with the contralateral third or oculomotor nerve. This arrangement of internuclear fibers is necessary to conform to the supranuclear control of the lateral conjugate movements. A distinction between these two, that is, the sixth cranial nerve and its nucleus, is, as Bing states, rather important.

Clinically, one can see why in some cases of infratentorial pathology, a paralysis of ipsilateral gaze may indicate an intrapontine sixth cranial nerve lesion; whereas, a paralysis of ipsilateral external rotation alone is a sign of extrapontine involvement of the sixth cranial nerve.

A somewhat similar analogy exists in the innervation of the so-called Bell's phenomenon. In this there is the demonstration of fibers arising in the oculomotor nucleus to pass through the medial longitudinal bundle, to the seventh nerve, joining it during its intrapontine course, and to pass along this nerve to supply the orbicularis oculi, the corrugator supercilii, and the frontalis muscles.

It has been impossible to find any mention, as a congenital syndrome, of the second of these two situations. Bielschowsky[9] discovered the first of these two situations and reported it. Walsh[1] also called attention to this variety and agreed with Bielschowsky that it is to be likened to, or included with, the jaw-winking cases as a similar syndrome. Bielschowsky, with others, also observed a reverse ipsilateral phenomenon, that is, a lowering of the upper lid rather than the

retraction of the upper lid—orbicularis rather than levator muscle contraction, though the possibility of levator muscle relaxation, as the associated movement, has equal likelihood.

The second of the two cases presented herein is that of contralateral upper-lid retraction. No reference can be found of this, up to the present, as a congenital situation. Wilbrand and Saenger's exhaustive Volume 1 of *Die Neurologie des Auges*, which deals with the eyelids, makes no mention of it at all. Other textbooks in English, French, and German, available for scrutiny, also fail to mention it.

Walsh[1] described one such case, unilateral in character, in a patient suffering from myasthenia gravis. This young lady, early in adult life, developed a weakness of the left upper lid with incompleteness of abduction in the left eye. When abduction (external rotation) was attempted, the right upper lid retracted. Walsh considered this retraction of the right upper lid to be a manifestation of the ordinary type of oculomotor secondary deviation consequent to the paresis of the left levator. His conclusion was sound; for it was based upon the disappearance of this contralateral lid retraction when the left eye (the eye with the paretic levator) was covered.

Figure 10 shows a similar appearance and it is not too difficult to assume that such a secondary deviation might also be present here and that this conjecture of Walsh might be the interpretation; even considering that this is a congenital defect.

It cannot be the reason, however, because of the marked elevation which appears in the left upper lid, when a normal right lateral rectus muscle is called upon for action. Figure 9 illustrates this beautifully.

One cannot ascribe it to a possible paresis of an internal rectus muscle, either, as seen here in the left eye (a phenomenon of misdirection of peripheral extrapontine fibers, similar to the pseudo-Graefe syndrome)—an intraneural third nerve association alone; for the internal rectus muscle on the right side seems wholly normal, and the associated reflex is definitely present therein as well.

Under such circumstances the increase, in the ptosis when combined with the paretic internal rectus muscle, would be an accompanying reciprocal denervation of the levator muscle which appears in left lateral rotation when normally a reciprocal denervation would appear in the internal rectus muscle of that side. It can hardly be an intranuclear third-nerve association, both levator and internal rectus muscles in the same eye (the same third nerve), because of the dissimilarity in the two internal rectus muscles, and the unilateral left-sided levator paralysis (or paresis)—hence, a gross dissimilarity in these two muscles or their innervation.

Conclusion

Up to the present time, six rather clear cut types of congenital pathologic oculomotor associated movements, or reflexes have been described. A seventh and an eighth acquired reflex are not uncommon findings. These latter two are the pseudo-Graefe syndrome or the misdirection of regenerating third-nerve fibers and the Bell's phenomenon.

Wartenberg attempted to place the locus of the pseudo-Graefe syndrome also in the supranuclear regions. The fallacy of this is quite evident when one considers the various lesions which account for this syndrome. One case was due to a compression sectioning of the third nerve at the apex of the orbit, and a second followed a classical hemiplegia alternans inferioris from an interpeduncular hemorrhage. These two cases are quoted as isolated instances of anatomic (as to position) extremes.

One of the congenital reflexes, the jaw-winking associated movement, with its 4 to 6 subclasses is the outstanding one. The remaining are: (2) the oculo-aural reflex described by Wilson,[10] in which lateral con-

comitant movements of the eyes are accompanied by a rotation of the pinna backward and toward the mastoid, the wider excursion of the ear being on the contralateral side; (3) the rather common oculofrontal reflex which results in an elevation of the ipsilateral eyebrow and a depression of the contralateral eyebrow with the concomitant lateral movements of the eyes; (4) the oculolingual reflex, wherein concomitant lateral deviations cause a deviation of the tip of the tongue toward the same side (homolateral, to the deviation of the eyes); and, (5) the oculomandibular reflex in which, according to Walsh,[1] "If the eyes are rapidly deviated to one then to the other side there may be protrusion of the mandible with the ocular deviation to the contralateral side." Vigorous contraction of the orbicularis muscles, also, will cause the reflex, as stated by Wartenberg.[4] It may be the same as the pterygocorneal reflex of von Sölder.[11]

The sixth reflex to be described is known as the orbiculostapedial, and was apparently first described by Carmichael and Critchley.[12] In this reflex, buzzing occurs in the ear ipsilateral to and with unilateral blepharospasm.

These reflexes are an association between the oculomotor nerves and/or the fifth and seventh cranial nerves. Actually, the first of these described (the oculo-auricular) has been used as a test[13] for determining the integrity of the facial nerve.

It seems as if another associated reflex can be added to this list of congenital associations just mentioned. It is perhaps best described as—an abducens-levator muscle associated reflex. Its etiology rests, possibly, in a congenital developmental nuclear defect. There is no proof that it arises from a supranuclear source; instead, the weight of evidence seems against that.

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GLAUCOMA AND ORALLY ADMINISTERED BELLADONNA*

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Until the time of von Graefe, glaucoma was generally recognized as incurable and establishment of its diagnosis was equivalent to a sentence of blindness. In 1857, von Graefe began to use iridectomy in cases of acute glaucoma and thereby inaugurated a revolution in ophthalmic surgery. Twenty years later (1876) Laqueur discovered that miotics were efficacious in controlling glaucoma.

It was de Wecker (1867-1901) who conceived glaucoma as a disturbance of the secretion and excretion of the intraocular fluid and attempted to relieve the condition by means of a filtering scar. Although he failed in his attempts, his work stimulated the research which led to the iridencleisis of Holth (1907), the cyclodialysis of Heine (1905), the sclerectomy of Lagrange (1905), and the corneoscleral trephining operation of Elliot (1909).[1]

While some men of the medical world were searching out the nature, mechanics, and treatment of glaucoma, it is likely that others were contributing to the incidence of glaucomatous blindness by prescribing belladonna in the treatment of nonocular conditions.

It is the purpose of this paper to show that acute congestive glaucoma may be precipitated and that preglaucomatous eyes may be exacerbated by the indiscriminate oral use of belladonna or its derivatives.

Linné named the deadly night-shade plant, Atropa belladonna, after Atropos, the oldest of the Three Fates, who severs the thread of life; belladonna means "beautiful lady," and this name originated from the fact that wide pupils were once considered marks of beauty and some women used decoctions of belladonna in the eyes to induce dilatation. Preparations of belladonna have been used for centuries and were known to the ancient Hindus.

Today, belladonna and its alkaloids have many therapeutic uses in medicine and surgery. Too often undesirable reactions are tolerated in order that a desired effect upon a given organ may be obtained. Tincture of belladonna (U.S.P.) and extract of belladonna (U.S.P.) are the two belladonna preparations most commonly used. The tincture contains an average of 30 mg. of the total alkaloids of belladonna leaf per 100 cc., or 0.15 mg. per 0.5 cc. (10 drops), the average dose. The extract contains 1.25 gm. of total alkaloids per 100 gm. or 0.1875 mg. per 0.015 gm. (0.25 gr.).

No figures are given for the relative amounts of the various constituent alkaloids of these standard preparations. The active constituents of the tincture and extract are chiefly atropine, hyoscyamine—the levoisomer of racemic atropine—and to a lesser extent, scopolamine.[2,3]

The belladonna alkaloids are rapidly absorbed from the intestinal tract and distributed throughout the body. Goodman and Gilman[2] state that atropine is in large measure hydrolized in the liver, and that one-third of the ingested dose is excreted by the kidneys, mainly within 14 hours. Sollmann[4] states that atropine is excreted, mostly unchanged, entirely by the urine, mainly within 36 hours.

The peripheral action of these alkaloids is directly on autonomic effector cells and not on nerve endings, producing in the eye, mydriasis, cycloplegia, and perhaps vasodilatation. This action may tend to elevate the intraocular pressure by the following mechanism: (1) Mydriasis tends to embarrass the filtration angle, (2) paresis of the ciliary

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muscle abolishes the pull of the radial fibers on the scleral spur with loss of the pumping action, (3) vasodilatation causes congestion and stasis.

Thus, atropine-induced glaucoma should be found in eyes with wide filtration angles as well as in eyes with narrow angles. In support of this is a case in which glaucoma occurred in an aniridic eye after the instillation of atropine in the eye (Duke-Elder).[1]

In the normal eye atropine mydriasis may be overcome by physostigmine (eserine) only after repeated instillation of 0.25-percent solution over a period of several hours. Hyoscyamine is twice as strong as atropine in its action on the iris (Sollmann).[4] Atropine easily overcomes the miosis of pilocarpine (Guyton).[5] In acute congestive glaucoma induced by topical atropine there may be no drugs which can overcome its effect (Duke-Elder).[1]

The amounts of atropine necessary to produce certain effects are as follows (Goodman and Gilman).[2] (It is assumed that these are ingested single doses because the author does not state otherwise.)

Milligrams	Grains	Reaction
0.5	1/120	Slight cardiac slowing; some dryness of the mouth.
1.0	1/60	Definite dryness of the mouth and thirst; slowing of heart rate, followed by some acceleration; mild dilatation of pupils.
2.0	1/30	Rapid heart rate; palpitation; xerostomia; inhibition sweating; some blurring of near vision; pupils dilated (but not quite immobile—Sollmann).
5.0	1/12	All above symptoms more marked; speech disturbed; difficulty in swallowing; dry, hot skin; headache.
10.0	1/6	Pulse rapid and weak; iris practically obliterated; excitement, restlessness; hallucinations; delirium and coma.

Mydriatic or cycloplegic glaucoma, due to the topical use in the eyes of atropine or other agents, is a tragic entity that has long been known in ophthalmic circles. It is infrequently seen. Abraham[6] reported its incidence as 0.0217 percent in patients over 30 years of age, but he also pointed out that mydriatic glaucoma is more common after the use of the longer-lasting mydriatics. His analysis included only cases of acute congestive glaucoma following instillation of mydriatics in the eyes. In Gradle's[7] series of cases in which mydriatics were used in the eyes, 0.9 percent of the eyes showed an increase of intraocular pressure under mydriasis, which led to further investigation, establishing the presence of a preglaucomatous condition.

It should be pointed out that the type of mydriatic glaucoma described by Abraham is infrequent because careful ophthalmologists constantly guard against it. The measures to prevent mydriatic glaucoma are given below and should precede the use of a mydriatic (Snydacker):[8]

Family history of glaucoma—blindness or more specific facts.

Personal history: (1) Halos around lights, (2) early morning headaches with or without blurred vision or halos, (3) ocular inflammation, (4) frequent changes of glasses, (5) medications patient is using.

Examination of the eye may reveal: (1) Small cornea, (2) shallow anterior chamber, (3) tendency to large pupils, reacting weakly to light and convergence, (4) glaucomatous cupping of the disc.

Tonometry, particularly after the age of 30 years, before and after the mydriasis (increase of 5 mm. Hg (Schiøtz) to be followed by complete glaucoma work-up).

Mydriasis for examination purposes should be controlled before patient leaves office, especially after the age of 30 years, bearing in mind that the effect of the mydriatic may outlast that of the miotic, causing mydriasis after the patient has left the office (Guyton).

Glaucoma after oral administration of belladonna

From the foregoing it is apparent that glaucoma due to the topical use of mydriatics in the eyes is a known entity, although apparently infrequent. However, the correlation of glaucoma and orally administered belladonna or its component alkaloids in the pure form, is not to be found in the literature. Duke-Elder quotes the case of Myashita, in which acute glaucoma followed the subcutaneous injection of atropine.

There are a number of conditions occurring in the glaucoma age group (40 to 70 years) in which belladonna preparations are administered by all routes in doses sufficient to produce mydriasis and cycloplegia, although mydriasis and cycloplegia are practically never as great as after the instillation of atropine or scopolamine solutions in the eyes.

Our report concerns six cases in which extract of belladonna or tincture of belladonna was given for gastrointestinal complaints, such as duodenal or peptic ulcers, ulcerative or spastic colitis, hyperacidity, or as a routine medication for psychosomatic complaints centered in the gastrointestinal tract. All of the patients except one were women with highstrung personalities who complained of sundry nervous symptoms. All of the patients were in the glaucoma age group, between the ages of 38 and 68 years, and five of the six had narrow filtration angles.

Since we did not examine any of these patients before the medication was given, no statement can be made as to whether the drug or a specific dosage had caused glaucoma, but in all cases the taking of the drug was followed within a few days to several weeks by eye symptoms, complaints of which the patient had not previously been aware.

It is worthwhile mentioning that none of the physicians who had prescribed the drug had given any thought to the possibility of ocular consequences or had questioned the patients as to possible past eye disease or eye treatment; nor did it occur to us in the Eye Department, prior to our first obvious case, to question the patients as to medication they had received during weeks or months prior to the eye examination. It is, therefore, within reason to assume that some cases of this nature may have been treated for glaucoma in our clinic without discovery of the fact that belladonna medication had previously been given by another physician.

When, within 10 months, we had seen these six cases in which glaucoma was clearly induced or aggravated by the internal use of belladonna drug, we began to do a little research into the method and frequency of belladonna uses in our own institution as well as in the community at large.

In our clinic an average of 4,000 outpatients are seen in a month. On the average, one out of 50 patients leaves the clinic with a prescription for belladonna in some form. The most frequently used prescription is: Extract of belladonna (0.015 gr.) and phenobarbital (0.015 gr.). One tablet 30 minutes before each meal. This formula, which is known as "Belap" or under similar patent names all over the country, gives one gr. of extract of belladonna per day. However, this prescription is frequently given with 0.5 gr. of belladonna 3 to 4 times per day.

If one out of 50 patients received this prescription at our clinic, about 80 patients were given it each month, approximately 800 patients in a period of 10 months. During the past 10 months we have seen somewhere between 22 and 26 cases of primary glaucoma. This figure does not include a single case of secondary, postoperative glaucoma. The reason that we cannot record an exact number of cases is because several hundred of our records were lost during the Vanport flood in May, 1948. Out of a series of, let us say, 25 cases of primary glaucoma, six, or approximately 25 percent, were induced or aggravated by the internal admin-

istration of belladonna. This is a high percentage indeed, and the more surprising since no mention of this subject can be found in the literature.

One of us then conducted a poll of several pharmacies in Portland, Oregon. It was learned that out of each 100 prescriptions dispensed for all reasons and by all physicians, excluding only prescriptions containing atropine or scopolamine used by ophthalmologists for the specific treatment of eye diseases, an average (the figures vary from 7 to 14 per 100) of 10 per 100 contained extract or tincture of belladonna (mostly extract), a fact which clearly indicates the frequency of its use as well as the nonchalance with which it is prescribed as a nonharmful drug. Moreover, let us note that the original prescription for "Belap" may be refilled without a new prescription in a number of states.

During these investigations it occurred to us that we had never observed any patient with Parkinson's disease, for which large amounts of belladonna or atropine in one form of another are prescribed, with glaucoma in any form. It would be interesting if this observation could be confirmed by other ophthalmologists. It would seem to indicate that patients with this disease, who for the most part are in the glaucoma age group, have a high tolerance to the drug in so far as precipitating glaucoma is concerned.

These observations and facts are being reported to stimulate further investigation in other and larger clinics. It is the ophthalmologist's concern to prevent cases of glaucoma and to educate other physicians so that they will not unwittingly contribute toward its occurrence or aggravation. If our observations are confirmed by others, steps should be taken by the Society for the Prevention of Blindness to have legislation enacted for putting Extract of Belladonna and Tincture of Belladonna under state law, so that prescriptions cannot be refilled without the order of a physician.

Case reports

Case 1

Mrs. C. G. was an emotionally unstable, white housewife, aged 52 years. She had a duodenal ulcer. For several months she had been taking tincture of belladonna, 10 drops, three times daily after meals. She complained of early morning bitemporal headache, slight photophobia, and inability to read more than a few minutes for months.

Eye examination. Pupils: Six mm. in diameter and equal, responded slowly and weakly to light and convergence. Fundi: Minimal hypertensive vascular changes. No cupping of optic discs. Accommodation was less than expected for the age of 52 years. She had a mild, compound, hyperopic astigmatism. Corrected visual acuity was: R.E., 20/20; L.E., 20/25. With a +2.5D. add for reading: R.E., J3; L.E., J2. Gonioscopy revealed very shallow anterior chambers, with a false angle in both eyes.

Ocular tension at 3 p.m. was: R.E., 28 mm. Hg (Schiøtz); L.E., 26 mm. Hg. The fields showed a slightly enlarged blindspot temporally and depression of the upper field for 1/1,000 white.

Course. The belladonna was discontinued and the patient was hospitalized for further study of the eyes. The ocular tension diurnal base line remained above 25 mm. Hg and the provocative water test was positive. She was placed on eserine (0.25 percent) at bedtime.

In two weeks the headache and the photophobia subsided. Visual acuity could then be corrected to 20/20 and J1 in each eye. The pupils were three mm. in diameter and responded briskly to light. From then on the ocular-tension readings remained below 25 mm. Hg. The fields gradually returned to normal over a four-month interval.

Case 2

Mrs. M. M., a 59-year-old white widow with a weight of 160 pounds, received extract of belladonna (0.25 gr.) orally, four times daily, after meals and at bedtime, for an "instable bowel syndrome." This patient was first seen, after she had taken a total of one gr. of the belladonna extract over a 24-hour period, to determine whether the eyes would tolerate the use of the belladonna.

Eye examination. Pupils: Three mm. in diameter, react briskly to light. Fundi show minimal hypertensive vascular changes; optic discs were normal in appearance. Accommodation was as expected for her age. She had a mild, mixed astigmatism. Corrected visual acuity was: 20/20, O.U. With a +2.0D. add: J1, O.U.

The anterior chambers were shallow; however, gonioscopy was not done in this case.

Ocular tension at 4 p.m. was: R.E., 23 mm. Hg (Schiøtz); L.E., 24 mm. Hg. Fields were essentially normal for 1/1,000 white and 4/1,000 red.

The patient was permitted to take extract of belladonna.

A recheck five days later showed that the patient was having early morning frontal headache. Pupils: Five mm. in diameter, reacted sluggishly to light.

Accommodation was diminished. There were minimal but suggestive field changes. Tension at 3 p.m. was: O.U., 26 mm. Hg (Schiøtz).

Belladonna was discontinued, and two weeks later the eye findings were about the same as on the first visit, and have remained so on subsequent visits.

CASE 3

Mrs. M. A., aged 38 years, was a hyperactive teacher who had been taking extract of belladonna tablets (0.25 gr.) three times daily after meals, for "spastic colon" for several weeks. Because she had fairly frequent attacks of migraine headache and undercorrected, moderate, compound hyperopic astigmatism, marked convergence insufficiency (determined after belladonna was discontinued) and a partial amblyopia of the left eye since childhood (20/60 with correction) the patient's symptoms of early morning headache and difficulty in reading were hard to evaluate.

Eye examination. Pupils: six mm. in diameter, responded weakly to light. Accommodation: R.E., 3.0 diopters; L.E., 3.5 diopters. This was less than expected for her age. Fundi: Essentially normal.

Ocular tension at 10 a.m. was: R.E., 30 mm. Hg (Schiøtz); L.E., 28 mm. Hg. Gonioscopy revealed fairly deep anterior chambers, but narrow angles. Fields: Right eye showed enlargement of the blindspot, with a tonguelike projection upward and downward from the blindspot and an incomplete arcuate scotoma above, with 1/1,000 white and 4/1,000, 8/1,000 red. The amblyopic left eye was not tested.

Belladonna was discontinued and the pupils, accommodation, and tension returned to normal in a few days, as did the central fields over a period of two months.

The following case is one in which acute bilateral glaucoma was precipitated by the use of oral belladonna:

CASE 4

Miss R. D., was a neurasthenic, unmarried, 68-year-old office worker. Her weight was 90 pounds. She had been taking extract of belladonna (tablets, 0.25 gr.), orally four times daily after meals and at bedtime for six days for a vague gastrointestinal complaint. (At the first visit for a checkup eye examination the history did not reveal the belladonna medication.) A diagnosis of chronic glaucoma had been made several years previously by another ophthalmologist, and pilocarpine (0.5 percent, drops 1), in each eye at bedtime had been used for the entire period. There had been no episode suggestive of acute glaucoma. The miotic had not been instilled for three days prior to the first visit.

Eye examination. Pupils: Three mm. in diameter, responded well to light. Fundi showed minimal arteriosclerotic changes. No cupping of discs was observed. Accommodation: R.E., 1.5 diopters; L.E., amblyopic since childhood. Correction of moderate hyperopia gave: R.E., 20/25; with a +2.5D. add, J1. There was comitant exotropia with the right eye leading. The patient stated that her eyes were crossed as a child and that the left eye turned out. Anterior chambers in both eyes were shallow. Central fields of right eye were normal for 1/1,000 white and 4/1,000 red. The amblyopic left eye was not tested.

Ocular tension at 10 a.m. was: R.E., 19 mm. Hg (Schiøtz); L.E., 16 mm. Hg.

It was planned to follow this patient for a time to determine whether she had a compensated glaucoma. Two days later the patient presented herself with a bilateral, acute, congestive glaucoma which could not be controlled by miotics. Within a few hours surgery was performed. An iridectomy ab externo was done on the left eye and attempted on the right eye, where it was unsuccessful because the scleral incision was too far posterior, not permitting iridectomy.

After surgery, the patient asked for her "tablets." It was then learned that she had been taking belladonna (0.25 gr.) four times daily after meals and at bedtime for eight days prior to the onset of the acute glaucoma.

Postoperatively, tension in both eyes remained low. Vision in the right eye did not improve beyond 20/50, and the eye was much less hyperopic due to anterior displacement of the iris lens diaphragm. The anterior chamber was very shallow. A filtering bleb developed at the site of the sclerotomy. The bleb plus topical use of eserine seemed to control the tension, and though there were marked glaucomatous field findings, postoperatively, for the right eye, there was no further change.

However, two and one-half months after the first acute episode, there was another acute attack in the right eye. Vision dropped to light perception only. Iridectomy ab externo was immediately performed. Vision has returned to 20/60. Tension has remained within normal limits for four months.

CASE 5

Mrs. V. H., a 52-year-old white saleswoman in a department store, was sent to the eye department on November 8, 1948, for examination to determine whether or not a preoperative atropine-sulfate injection for removal of a uterine polyp would be proper.

Eye examination. There was deep cupping of both discs, especially in the left eye, with a tension of: R.E. 23 mm. Hg (Schiøtz); L.E., 25 mm. Hg. Since the patient was already prepared for operation on the following day, a careful eye examination was scheduled for after the operation. On November 12th, the patient was seen in the eye department, and a few changes were found.

There was a pronounced nasal step on the left eye, and she was put on eserine. On December 2nd she returned with acute complaints. In the left eye the cupping was deeper and more extensive than

previously, and the tension in this eye was found to be 54 mm. Hg.

A detailed history of this case revealed that the patient had consulted our medical department in August, 1948, because of vague gastrointestinal complaints and was given a prescription for extract of belladonna (0.25 gr.) four times a day, which she took for 4 or 5 weeks. About two weeks after taking the drug she began having difficulty in reading and went to the optometrist to have her glasses changed. She had never complained about her eyes prior to consulting the doctor for her stomach trouble and has never found relief for her eye trouble since.

CASE 6

Mr. C. W., a 66-year-old white man, had suffered from peptic ulcers for several years. He was hospitalized for this reason for several weeks in September, 1948, and received treatment with tincture of belladonna, 10 drops three times a day. At discharge, he was given this prescription and advised to continue this medication. On November 2nd, while still taking belladonna, he was seen in the eye department.

Eye examination. Vision was: R.E., 20/200; L.E., 20/30, not correctible with glasses. Pupils: Moderately dilated. Fundi showed well-advanced arteriosclerosis, with a marked cupping in the right eye and some pigment degeneration in the macula of that eye.

Ocular tension was: R.E., 30 mm. Hg (Schiøtz); L.E., 23 mm. Hg. Field changes in the right eye could not be established because the vision was too poor. He was put on eserine and advised an operation, which he refused.

CASE 7

Mrs. H. B., was a very apprehensive 18-year-old stenographer. Her weight was 130 pounds. She had been taking extract of belladonna tablets (0.25 gr.) three times daily for an asthmalike hysteria for six days. She had complained of difficulty with near vision for three days.

Eye examination. Pupils were dilated and responded weakly to light and accommodation. Accommodation: R.E., 4.5 diopters; L.E., 3.0 diopters. Correction of slight simple myopia in the left eye gave 20/20 vision in each eye. Fundi and central fields were normal. Gonioscopy was not done.

Ocular tension at 3:30 p.m. was: R.E., 23 mm. Hg (Schiøtz); L.E., 24 mm. Hg.

Belladonna was discontinued.

Six days after the belladonna was discontinued the pupils were still large, but reacted quickly to light. Accommodation was 11 diopters in each eye. Ocular tension was 18 mm. Hg in each eye at 3 p.m. Fields remained normal. On subsequent visits the ocular tension remained around 18 mm. Hg in each eye and the other findings remained about the same.

This case is presented to show the effect that ingested belladonna has on the pupils and accommodation. It is omitted from our statistics.

SUMMARY

1. A brief discussion of the pharmacology of the belladonna alkaloids is presented with particular attention to their effects on the eye.

2. Mydriatic glaucoma due to topical use of mydriatics in the eyes is discussed. The absence of literature correlating glaucoma with orally administered belladonna alkaloids is pointed out. This correlation is made in this paper.

3. Prophylactic measures against mydriatic glaucoma are restated from the literature.

4. Six cases are reported to show that ingested belladonna exacerbates preglaucomatous eyes.

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CHOICE OF OPERATION IN ACUTE GLAUCOMA SECONDARY TO SWELLING OF THE LENS*

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Choice of operation for an eye in which the glaucoma is said to be secondary to lenticular swelling is a problem which at one time or another confronts every ophthalmic surgeon. The literature contains scant reference based on statistical evidence as to the operative procedure or procedures to be done in these cases.

In cases of primary glaucoma plus cataract, which is not precisely the type of glaucoma under discussion, Elschnig[1] and van Lint[2] advise that a cataract extraction should be the first operation if the intraocular pressure rises above 35 mm. Hg and can be reduced to 20 mm. Hg with miotics; otherwise a cyclodialysis is to be done, and this is to be followed by a lens extraction in four weeks. Spaeth[3] believes that a preliminary iridectomy should be performed and followed at a later date by a cataract extraction.

Kirby[4] thinks that a cataract extraction should only be performed if the intraocular pressure is normal. If the intraocular pressure is above normal, he performs an anterior fistulizing operation at least six weeks before a cataract extraction. If the intraocular pressure is still elevated, a second antiglaucoma operation is done prior to cataract surgery. If the intraocular pressure is normal at the time of cataract surgery, the filtering area is avoided by making the corneal section in front of the bleb; however, if hypotony (8 mm. Hg or below) has resulted following the fistulizing operation, the section is made through the area of the bleb in the hope that the intraocular pressure will rise to within normal limits on healing.

O'Brien[5] feels that an anterior sclerectomy should be done at the time of the cataract surgery. Guyton[6] draws the following conclusions: "If the glaucoma is noncongestive and cannot be controlled with miotics, an anterior fistulizing operation should be performed prior to cataract extraction. If the glaucoma is noncongestive but can be controlled with miotics, or if it is chronic congestive, a combined cataract extraction should be the initial procedure and is likely to be the only operation necessary."

GLAUCOMA SECONDARY TO LENTICULAR SWELLING

The present discussion, however, deals with the eye in which the glaucoma is said to be manifestly secondary to lenticular swelling. Is the lenticular intumescence primarily responsible for the severe rise in intraocular pressure or is the eye a truly preglaucomatous eye in which the lenticular swelling acts as a "natural" provocative test in causing the acute glaucoma?

It is common knowledge that in many eyes which come to cataract surgery the swelling of the crystalline lens has not had an abnormal effect on the balance of the intraocular pressure. It is unusual to see an eye in which the lenticular intumescence has given rise to an attack of acute glaucoma. That type of senile cataract that passes through the intumescent stage in its development, does so uneventfully, as a general rule, in so far as the intraocular pressure is concerned.

FINDINGS IN NONGLAUCOMATOUS EYE

To study the matter further, we also carefully observed the opposite eye in the patients who had developed an acute glaucoma secondary to lens swelling to determine the presence of an anatomic or physical predisposition to acute glaucoma.

In our cases, gonioscopic examination has

* Presented before the Chicago Ophthalmological Society, December, 1948.

shown that the angle of the anterior chamber of the eye opposite to that of the one with lenticular swelling is of the narrow type. Furthermore, the eye reveals an anatomic predisposition to acute glaucoma—the hyperopic type of refractive error (shortness of eyeball), the shallow anterior chamber as noted on biomicroscopic examination (relatively small cornea and anterior segment), and the other anatomic and mechanical factors generally given in a description of classical narrow-angle glaucoma.

Findings in glaucomatous eye

The eye which manifests the acute glaucoma due to lenticular intumescence reveals the classical findings of acute glaucoma in the congestive phase—superficial and deep ciliary vessel congestion, edema of the cornea, shallow anterior chamber, and a more or less dilated pupil. Gonioscopic examination can usually be done following clearing of the corneal edema by glycerin. This reveals an extremely narrow entrance to the angle, so narrow in fact that details frequently can not be seen over the iris lenticular hump.

Postoperative gonioscopic examination, however, has revealed peripheral anterior synechias. The extent and firmness of these peripheral anterior synechias seem to be in direct proportion to the duration of the congestive phase of the acute glaucoma. It is these findings which lead to the belief that the lenticular intumescence acts as a "natural" provocative test or as the provoking insult in a truly preglaucomatous eye.

The anatomic predisposing factors present in these eyes, plus the swelling of the crystalline lens, increase the shallowness of the anterior chamber and the narrowness of the angle, so that entrance to the angle becomes too narrow and the normal intraocular pressure can no longer be maintained.

Miotic therapy

These eyes usually do not respond to any type of miotic therapy; presumably because the mechanical factors which cause the angle crowding cannot be eliminated. These factors, together with the vascular decompensation which is present, and the congestive effect of the miotic drug, initiate a vicious circle.

Choice of operation

The choice of operation, therefore, resolves itself into the treatment of the acute glaucoma.

Sugar[7] has shown that the angle of the anterior chamber is open but narrow prior to the first attack of acute glaucoma, but that peripheral anterior synechias develop during the attack and vary in extent directly with the duration of the attack. Therefore, if the patient can be operated within the first 24 hours of an attack, a basal iridectomy may be done.

It is necessary to enter the anterior chamber in such a way as to cause minimum danger to the iris and the capsule of the lens, and to avoid sudden decompression of an eyeball in which the intraocular pressure is high.

This can be done by making a scratch incision or an incision ab externo from the outside after a conjunctival flap has been dissected to the limbus. This scratch incision can be bevelled to any degree in order to enter an anterior chamber with an extremely narrow angle. The incision may then be enlarged with the corneal scissors. This type of incision provides for slow decompression and, ordinarily, prolapse of iris tissure occurs.

If surgery is performed during the first 24 hours of the attack, the lens extraction may be done immediately following the iridectomy, since the synechias are, as yet, neither extensive nor firm. However, it is felt that the additional insult of the lens extraction upon the vascular tissues (ciliary body) of an already irritated eye is not justified. Lens extraction at this time may increase the risk of postoperative glaucoma, since additional peripheral anterior synechias may develop if, for any reason and in

spite of the use of corneoscleral sutures, there is delay in the reformation of the anterior chamber.

Ordinarily the patient with an acute glaucoma secondary to lenticular intumescence is not seen within the first 24 hours. Since it may be assumed that peripheral anterior synechias are now fairly well developed, it would seem that a filtering operation would be the procedure of choice. The iridencleisis operation is certainly preferred for narrow-angle glaucoma. The effects of the narrow angle offer sufficient mechanical hazards during operation and afterward to make trephination a poor choice in this type of glaucoma. It is necessary that the trephine opening be placed sufficiently anteriorly in the cornea to avoid the formed peripheral anterior synechias and ciliary incarceration, and this in itself is difficult.

The anatomic choice for the antiglaucoma filtering operation is the superior limbus, for the sclera envelops the cornea here to a greater extent; in addition the root of the iris lies farther behind the corneoscleral junction here than at any other point of the corneoscleral circumference.

This provides for a conjunctival flap farther forward on the cornea, with the result that the incision may be made into a broader portion of the angle of the anterior chamber and damage to the iris, or to the lens capsule, which in turn may lead to further swelling, is thereby avoided. For this reason it is preferable to do the filtering operation at the upper limbus and to make the incision for the subsequent cataract extraction inferiorly or temporally, or, as Kirby[4] chooses, anterior to the filtering bleb. The incision sometimes cannot be made through the cornea and then entrance to the anterior chamber for the antiglaucoma surgery is accomplished by a scratch incision from the outside as has already been described.

Cataract extraction

The use of corneoscleral sutures is certainly strongly advised for the cataract surgery. The lens extraction may be done when the postoperative reaction of the antiglaucoma surgery has subsided and the eye is pale. Ordinarily, the cataract surgery may be performed after a period of six weeks. The intracapsular lens extraction is the operation of choice. This may be accomplished either with the lens-capsule forceps or with the erisophake. The erisophake must be used if the swelling of the lens is sufficient to prohibit the grasp of the lens capsule by the forceps. However, it has been found that the lenticular intumescence frequently diminishes following control of the intraocular pressure so that the capsule may be grasped by the forceps and the lens delivered intracapsularly. The zonular fibers seem to rupture more easily after an acute attack of glaucoma.

Case reports

A brief résumé of several cases follows. The intraocular pressure of our cases has been within normal limits following the antiglaucoma and cataract surgery, in each case without the use of miotics.

Case 1

Mrs. B. J. M., aged 49 years, had an intracapsular cataract extraction in the left eye in August, 1943. Prior to the lens extraction it was noted that the anterior chamber appeared somewhat shallow and there was a narrow entrance to the angle.

On May 31, 1946, this patient was seen with an acute glaucoma of the right eye of two days' duration. The pupil was seen to be dilated and an intumescence of the lens was seen with the slitlamp. The anterior chamber was extremely shallow and the details of the angle could not be observed gonioscopically. Intraocular pressure was: R.E., 52 mm. Hg; L.E., 20 mm. Hg (Gradle-Schiøtz).

The patient was placed on intensive miotic therapy, but three days later the intraocular pressure of the right eye was 42 mm. Hg and an iridencleisis was performed with an incarceration of the iris pillar. Four months later, an intracapsular lens extraction was done with the incision placed in the lower two fifths of the limbus. The corrected vision is now 20/20 and the intraocular pressure has remained within normal limits without the use of miotics.

The intraocular pressure of the left eye has always been normal.

CASE 2

Mrs. S. L., aged 64 years, was first seen in April, 1947. There was a history of a gradual loss of vision of each eye during the past two years. Diabetes mellitus, present for four years, was controlled by dietary measures. The vision of each eye at this time was light perception and projection.

Examination of the right eye showed the cornea to be somewhat small, the anterior chamber to be shallow, and the entrance to the angle of the anterior chamber was narrow. Slitlamp examination showed a mature, grayish-white cataract. No fundus details could be seen.

In the left eye, the cornea was small, the anterior chamber was very shallow, and the entrance to the angle was narrow. Slitlamp examination showed a complete opacification of the lens with intumescence so that the anterior chamber seemed almost obliterated. The intraocular pressure at this time was 22 mm. Hg (Schiøtz) in each eye. An extraction of the right lens was advised.

Two days later, however, the intraocular pressure of the left eye became hard and did not respond to intensive miotic therapy of 24 hours' duration. An iridencleisis was therefore done. Because of the shallow anterior chamber, an ab externo incision was made. The opposite eye was placed on miotics as a preventive measure. An intracapsular lens extraction was performed on the right eye a week later without incident, an intracapsular cataract extraction was performed in the left eye in November, 1947. The incision for the extraction of the lens was made in the lower two fifths of the limbus. The McLean type of corneoscleral sutures was used. The intraocular pressure of each eye is normal without the use of miotics at the present time.

CASE 3

Mr. A. E. C., aged 73 years, had an intracapsular lens extraction on the left eye in November, 1945. Corrected vision is 20/20. The intraocular pressure of this eye has been normal.

In December, 1947, this patient was seen with an acute glaucoma of the right eye of four days' duration. The anterior chamber was so shallow that details of the angle could not be seen with the gonioscope. The pupil was seen to be dilated to 5 to 6 mm. and an intumescence of the lens was noted with the biomicroscope. The intraocular pressure at this time was 32 mm. Hg in the right eye, and 17 mm. Hg in the left eye (Gradle-Schiøtz). The right eye was put on intensive miotic therapy and the intraocular pressure promptly returned to within normal limits.

In spite of the continuation of the miotics, the right eye developed a second attack of acute glaucoma five days later and an iridencleisis was promptly done. In June, 1948, an intracapsular cataract extraction was performed with the incision placed in the cornea anterior to the site of the iridencleisis bleb using two McLean-type sutures. The intraocular pressure of each eye has been within normal limits without miotics.

CASE 4

Mrs. B. K. L., aged 57 years, was first seen in April, 1945. She gave an initial history of a gradual loss of vision for several years, more severe in the left eye.

Ocular examination revealed each eye to have anterior chambers which were somewhat shallow and the entrance to the angle was narrow in each eye. In the left eye, peripheral anterior synechia was seen in the superior third with the gonioscope. The intraocular pressure was 17 mm. Hg in the right eye, and 38 mm. Hg in the left eye (Schiøtz).

The visual field of the right eye was essentially normal while the visual field of the left eye showed a superior arcuate scotoma within 15 degrees of fixation with a Roenne step.

The patient was placed on a two-percent pilocarpine nitrate, four times daily, in each eye. After two days the intraocular pressure was 15 mm. Hg in the right eye, and 34 mm. Hg in the left eye (Schiøtz). An iridencleisis was advised for the left eye and performed five days later. The intraocular pressure of this eye has remained within normal limits without the use of miotics.

In August, 1947, the patient was seen with an acute glaucoma of the right eye of a day's duration despite the continued daily use of pilocarpine and frequent visual and tonometric checks of the glaucoma. Nevertheless, at this time, the pupil was seen to be dilated to five mm.; the anterior chamber was very shallow, and lenticular intumescence was noted with the slitlamp. The intraocular pressure of the eye was 52 mm. Hg (Schiøtz).

The patient was placed on more intensive miotics for 24 hours and, since there was essentially no response, an iridencleisis was then done.

An intracapsular lens extraction was performed three months later with the incision placed in the cornea just anterior to the bleb. Two McLean-type sutures were used to close the incision. The intraocular pressure has remained within normal limits without the use of miotics. The corrected vision of this eye is 20/20.

COMMENT

This series of cases is too small to allow dogmatic conclusions. Nevertheless, it does indicate that eyes in which the increased intraocular pressure is said to be secondary to lenticular intumescence are of the preglaucomatous narrow-angle type which have suffered an acute rise in pressure as a result of the increase in the narrowness of the entrance to the angle from the development of the lenticular swelling.

The subsequent acute congestive glaucomatous phase does not usually respond to miotic therapy. An anterior fistulizing operation, preferably an iridencleisis, ap-

pears to give excellent results in our hands. Subsequently, the cataract extraction may be performed, with an incision placed either inferiorly or anteriorly to the site of the antiglaucoma surgery and with the use of corneoscleral sutures.

An iridectomy may be the initial antiglaucomatous procedure if the acute congestive attack is seen very early in the first attack and prior to the development of extensive peripheral anterior synechias.

We have hesitated to extract the lens in an eye undergoing an acute congestive attack of glaucoma because we believe it is unsound surgery to extract a lens in a red, irritable eye, thereby adding trauma to an already irritated ciliary body.

Moreover, the possibility of or the presence of peripheral anterior synechias prior to the cataract operation plus the possibility of the development of further peripheral anterior synechias during the immediate postoperative period following cataract surgery should preclude the extraction of the lens during an acute congestive attack of glaucoma.

Since we believe that the lenticular swelling acts as a "natural" provocative test in a truly narrow-angle, preglaucomatous eye, it seems to us advisable to initiate the use of miotics in the eye opposite to that in which glaucoma secondary to lens intumescence has developed. If at any time, there is a suggestion of the development of an acute congestive attack or if the base intraocular pressure remains high despite the use of miotics in this type of glaucoma (the narrow-angle type), we believe a basal iridectomy should be performed.

Furthermore, the lens extraction in the eye opposite to that developing an acute glaucoma secondary to lenticular intumescence should not be delayed unnecessarily if lenticular changes are sufficient to account for decrease in vision.

Discussion

Cataract and glaucoma may be associated in the following combinations:

1. Cataract and glaucoma may occur simultaneously. These none too rare cases may be very serious for the individuals concerned, because, as a rule, they consist of a compensated or deep angle glaucoma accompanied by a gradual onset of the cataract. If the glaucoma is not diagnosed early, marked deterioration of the visual functions will have occurred before the lens extraction takes place.

The type of surgical interference depends upon the degree of tension present and the condition of the iris.

If the intraocular pressure is only moderately elevated, under 35 mm. Hg, and can be lowered to normal (under 20 to 25 mm. Hg) with miotics, and the iris is normal, a primary lens extraction combined with an iridectomy is indicated. If the anterior chamber is very shallow, the incision should be made ab externo with a scalpel.

If the intraocular pressure is higher, and the iris atrophic, and there are signs and symptoms of an acute congestion, or there has been a history of a previous attack and the symptoms cannot be alleviated or controlled by the use of miotics, then a cyclodialysis is indicated, to be followed within 5 to 6 weeks by a lens extraction. In the presence of an atrophic iris, one should hesitate to perform an iridencleisis.

2. However, the subject under discussion has to do with acute glaucoma accompanying or following cataract formation or a swelling of the lens. Occasionally a spontaneous subluxation of a hypermature senile cataract may result in the onset of an acute glaucomatous attack. More frequently, the swelling of a maturing cataractous lens, occurring in a shallow-angle chamber in a so-called predisposed eye, may cause sufficient embarrassment to the tension-regulating mechanism to precipitate an acute glaucomatous attack.

This type of glaucoma differs materially from that just mentioned and necessitates a different type of operative interference. If

the intraocular pressure is only moderately elevated and the acute glaucoma responds to miotics (which did not occur in our series of cases), then a primary lens extraction combined with iridectomy is indicated. The presence of a shallow chamber may necessitate the use of an incision ab externo with a scalpel.

If there is a greater elevation of tension and it cannot be lowered by the use of miotics, an iridectomy should be performed within the first 24 hours after onset of the attack. After this period of time, an iridencleisis is indicated, to be followed in about six weeks by a lens extraction. Elschnig recommended a posterior scleral puncture to be followed by a lens extraction 1 to 3 hours later, when the anterior chamber has deepened.

There are occasional cases in which the spontaneous rupture of the capsule of a morgagnian cataract results in the onset of a severe acute congestive glaucoma accompanied by cyclitic changes, such as posterior corneal precipitates, fibrin formation in the anterior chamber, and so forth. The prognosis in such cases must be guarded.

They are probably best handled by anterior-chamber puncture at the lower limbus, followed by a lens extraction and iridectomy the next day.

3. Cataract formation may result from the presence of glaucoma (cataracta glaucomatosa). As a rule in this stage, there is a degenerative absolute glaucoma, and intraocular antiglaucomatous surgery is contraindicated. One must then resort to cyclodiathermy puncture or, eventually, enucleation.

As a rule, in these cases there is an increase in the vitreous pressure, so that there is more likelihood of vitreous loss during the extraction of the lens. It is possible that venesection may be effective in preventing this complication.

Pilocarpine should be instilled both in the operated and nonoperated eye following operative interference.

Summary

Choice of operation for an eye in which glaucoma is secondary to lenticular intumescence is discussed.

It is believed that the acute congestive glaucomatous attack which is said to be secondary to lens swelling occurs in an eye which may be termed preglaucomatous. The opposite eye is frequently preglaucomatous in type with a narrow entrance to the angle of the anterior chamber.

An iridectomy with lens extraction, if done early, and, if done later, the iridencleisis alone are the operative choices for reducing the increased intraocular pressure. An intracapsular cataract extraction is performed subsequently with the use of corneoscleral sutures if iridencleisis was the antiglaucomatous procedure.

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FLICKER FUSION FIELDS*

I. The Effect of Age and Pupil Size

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In my initial study of flicker fusion frequency,[1] it was shown (fig. 1) that the critical fusion rate decreased abruptly with decrease in pupil size. This was reasonable, because flicker fusion frequency (F.F.F.) depends upon, and is proportional to the log intensity of the target light. The average curve in Figure 1, is parallel to Sloan's curve[2] to show the increase in absolute light threshold with decreasing pupil size, and is similar to Speiser's[3] curve on flicker fusion frequency.

This effect on flicker fusion frequency of pupil size impressed me so, that all of the patients examined for flicker fusion frequency have had pupil size under test conditions recorded with the flicker field. Pupil size was determined roughly by comparison to a standard, and recorded as the nearest round number, in millimeters. As more and more controls and patients were tested, however, it became apparent that many with naturally small pupils had high flicker fusion frequency.

As early as 1929, Lythgoe and Tansley[4] measured flicker fusion frequency with subjects having different natural pupil size, and concluded that pupil size was insignificant.

Karpe,[5] 1945, in his monograph, stated that in many cases there was no difference in the electroretinogram, with miotic or dilated pupils.

Weekers,[6] 1946, reported reduced flicker fusion frequency fields in all older patients which he believed due to reduced pupil diameter.

Speiser,[3] 1948, studied flicker fusion frequency with 10 subjects whose pupils were varied by homatropine and pilocarpine. She used the mechanical sector disc method, central fixation, and a small medium intensity target. With pupils of 8 to 9 mm., F.F.F. was 39 : 3 to 4, 29 : 2, 24 (fig. 1).

Ferree, Rand, and Sloan,[7] 1934, reported the effect of pupil size on form and color fields. Changes in fields after miosis with pilocarpine were insignificant. There was 1.4-degree field decrease with the one-degree white target. For one-degree red, the field was enlarged slightly for two hypermetropes with miosis. Larger test objects had even less effect on fields. Since flicker fusion frequency is not dependent on form vision or acuity, this work does not apply to the present problem.

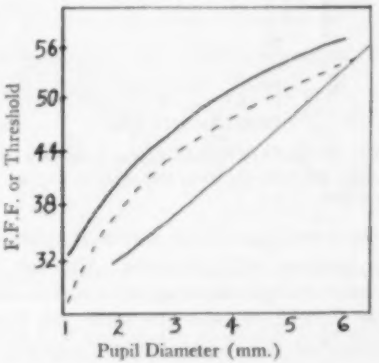

Fig. 1 (Miles). Solid curved line: Average flicker fusion frequency with artificial pupils of 10 light-adapted eyes.[1] Broken line: Reciprocal of light threshold of the dark-adapted eye for various artificial pupil sizes, Sloan.[2] Solid straight line: Average flicker fusion frequency of 10 subjects treated with homatropine and pilocarpine, Speiser.[3]

The filter experiment

If flicker fusion frequency depends on pupil size, all flicker fields should be performed with pupils of uniform size. This

* From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

obviously is impractical for clinical purposes. An alternative is to vary the intensity of the target and surround. This was done by means of neutral gray glass filters calibrated to equate any sized pupil to two mm. Flicker

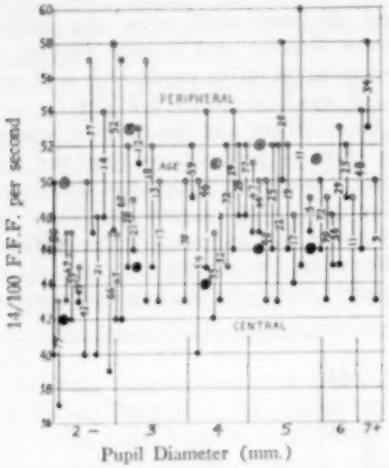

Fig. 2 (Miles). Flicker fusion frequency in 48 normal subjects, showing the relation of age and pupil size.

fields were taken on six normal controls and six patients with glaucoma. Although the amount of light striking the retina in each case must have been the same, the filters diminished the flicker fusion frequency so markedly that the results were worthless.

The experiment, however, gave a clue to the conflicting results reported in the literature. Evidently, time is required for the eye to adapt itself to the reduced illumination, whether from a miotic pupil or from a filter. Rather than have the patients sit with gray filters before the eyes for an hour prior to the test, it was decided to study a group of controls of different natural pupil size, adapted to ordinary waiting-room illumination, about five foot-candles.

Method

The flicker target consisted of a disk of thin white paper, illuminated from behind by a gas discharge tube. An electronic instrument turned the light completely on and completely off for an interval of 0.010 seconds at any desired frequency to be read from a dial. The target was white, tinted with red and orange, and deflected a photoelectric meter in direct contact, without shield, six foot-candles in Series I; 10 foot-candles in Series II. In Series I, the target was 14 cm. in diameter and in Series II, five cm. The background was gray in color with incident light measuring about two foot-candles, enough that the patient's pupils could be observed. The target was viewed monocularly at one meter.

The flicker fusion frequency was first determined centrally, by having the patient look at the center of the target, and report "now" when the light first began to flicker

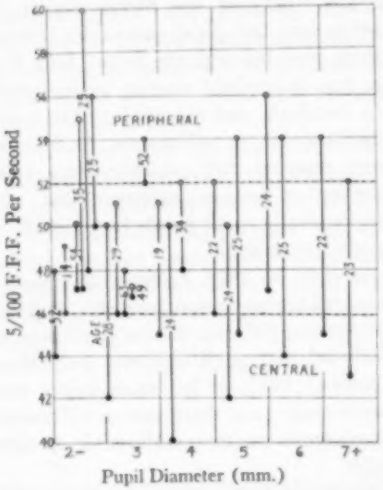

Fig. 3 (Miles). Flicker fusion frequency in 21 normal subjects, showing the relation of age and pupil size.

as the frequency was reduced slowly. The average of three determinations was recorded, although there was little or no variation.

Peripheral readings were taken with the

patient fixing 10 degrees laterally, to stimulate temporal retina. When readings differed in the two eyes, the higher was taken for these series.

Results

Figure 2 shows the flicker fusion frequency in the first series of 48 subjects, compared to age and pupil size. Of the nine who had pupils two mm. or smaller, the average central flicker fusion frequency was 42, the peripheral, 50 flashes per second. All those with larger pupils averaged about the same, only three flashes higher. There was little correlation with age.

Figure 3 shows similar results on 21 subjects tested on a smaller, more intense target. In the six having pupils of two mm. or smaller, the average central flicker fusion frequency was 47, the peripheral, 53. Those with larger pupils averaged central, 46; peripheral, 51.

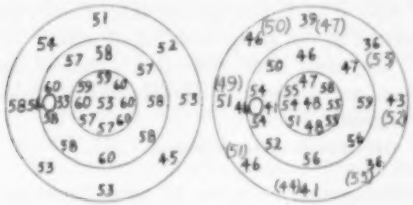

Fig. 4 (Miles). Flicker fusion fields in a normal subject before and after miosis with pilocarpine. Pupil change was from 5.0 to 1.5 mm. Second field was taken one hour after miosis. Figures in parenthesis show change after two hours.

Many older subjects with two-mm. pupils were found to have lower flicker fusion frequency, and were not used in this chart. Therefore, statistically, Weekers[6] was right in saying age lowers the flicker fusion frequency. Figures 2 and 3 show quite normal flicker fusion frequency values in nine subjects above the age of 60 years. These must be free from the common senile retinopathies.

There is great individual variation in flicker fusion frequency, as there is variation in sensory perception in general.

Figures 4, 5, and 6 show flicker fields in normal subjects with variation due to extreme differences in pupil size. Figure 4 shows on the left, the field of an eye with the natural diameter of the pupil, five mm. One-half hour after miosis with pilocarpine, this field was depressed generally about one-third. Figure 4 on the right shows the field in the same eye after one hour, and (in parentheses) the peripheral field after two hours. Apparently about two hours are required to permit adaptation so that flicker fusion frequency returns to normal. This must be dark adaptation, but not in the ordinary sense. Pupil size may change light intensity about 24 fold, but the eye dark-adapts to a change about 100,000 fold.

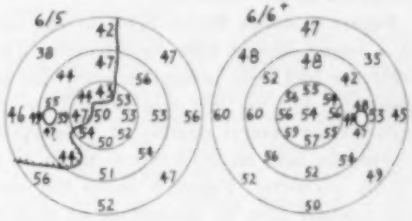

Fig. 5 (Miles). Flicker fusion fields in a normal subject with one pupil miotic due to trauma in childhood. Depressed quadrant, O.S., is due to anterior synechias.

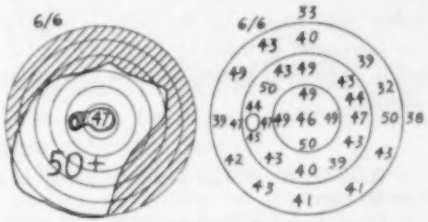

Fig. 6 (Miles). Flicker fusion fields, left eye, of patient with buphthalmos on pilocarpine. There had been no sign of glaucoma, this eye. The left field, August, 1948, was taken by a method to be described in a later paper. The tangent screen field, January, 1949, is likewise normal.

The subjects described here were adapted for an hour or more to waiting-room illumination. In complete dark adaptation, flicker

fusion frequency drops to from 12 to 20, and all higher readings represent cone activity.

Figure 5 shows that a naturally miotic pupil depresses the flicker field an insignificant amount, more centrally than peripherally, compared to the fellow eye.

Figure 6 shows flicker fields in one eye of a young subject with buphthalmos. The right eye had light perception only, due to glaucoma, but the left was normal by all tests. After several months of pilocarpine miosis, the field on the left was taken on a 50-cm. perimeter. Figure 6 shows the normal annular area of perception of flicker, kept at a constant rate of 50 flashes per second as the target is exposed to various parts of the retina. The normal central relative scotoma flicker fusion frequency is 47. The flicker field shown on the right is slightly low compared to those of Figures 4 and 5, but is considered normal because of regular contours.

Summary and Conclusions

Previous work on the effect of pupil size on flicker fusion frequency indicated that the rate drops markedly with decrease of pupil diameter. Before flicker fusion frequency can be used clinically this point must be clarified.

Experiments described in this paper show that the change in flicker fusion frequency with pupil size described in the past was due to insufficient time permitted for complete adaptation to the reduced illumination.

Fifteen normal subjects with pupils naturally two mm. or less in diameter were compared with 44 subjects who had pupils of larger size. The average flicker fusion frequency both central and peripheral was found to be depressed only three flashes per second in the group with small pupils.

The same data show that advanced age does not necessarily depress flicker fusion frequency.

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HEADACHE AS A SYMPTOM OF VISUAL DISABILITY

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PAIN

Pain may be superficial or deep. Superficial pain is felt as a pricking, burning, or cutting sensation, directly at the site of stimulation. Deep pain is aching, throbbing, and numbing in character. It may be felt at the point of the stimulus. More often deep pain is felt in areas other than those stimulated. This is so because the nervous excitation spreads along the neurones to other portions of the same neural segment, or to adjoining segments. This pain stimulus reaches the perception centers via nerves, the terminal elements of which were never stimulated; and pain is felt in a new location. The process is called pain referral.

In referred areas of pain two things can happen:

1. The perception of noxious stimuli may be more acute in areas of referred pain. This is a central mechanism. The term applied to describe the phenomenon is hyperalgesia. Stimulation of an hyperalgesic area of referral may produce more discomfort than stimulation of a normal area.[1]

2. Skeletal muscle contracture in a referred area, due to excitation spread along motor nerves of the same segment, may occur.[1] This contracture may be great enough and sustained long enough to produce painful stimuli in itself. Thus, in a site of referred pain may be set up secondary effects which become more painful than the original injury.

HEADACHE

Headache, as distinguished from pain on the surface of the head is referred pain. All of the structures capable of producing headache experimentally, as well as clinically, are subsurface or intracranial and, therefore, must be considered deep. This would include the contents of the orbits, the sinuses, the extracranial arteries, and the frontal, temporal, occipital, and posterior cervical muscles.[2]

Hyperalgesias are especially common about the head, and complicate the picture of referred pain. Likewise, contracture of scalp and posterior cervical muscles bring added pain. The build up from a comparatively insignificant original stimulus may be such that the resulting headache is incapacitating.

EYE HEADACHE

Experiments have shown that pain can be aroused from traction on the extraocular muscles, or from the ciliary muscle and iris. It is also felt that increased tension of scalp muscles (probably as a referred phenomenon in the struggle of difficult vision) may cause many headaches.[3]

We are all aware that powerful miotics produce constriction of the iris sphincter muscle and spasm of the muscles of accommodation; and that brow headaches almost invariably accompany the drug action. This is certainly an example of referred pain because the primary pain stimulus comes from the intraocular musculature.

Moench suggests that refractive errors, muscle imbalances, accommodative and convergence excess cause ocular headaches, and suggests areas of localization for the different types.[4]

There are no satisfactory statistics available on the incidence of headaches in the general medical population. Estimates run as high as 50 percent.

Hersh reviewed 6,000 cases referred for headaches to the Eye, Ear, Nose and Throat Department of Camp Stoneham Hospital, one third of which had a presumptive diagnosis of refractive error. Actually only 35 patients were found to have eye disorders,

and only 11 had primary visual problems without pathologic conditions.[8]

Statistics

Recently from my practice I tabulated 434 cases that had been examined because of visual complaints exclusive of pathologic conditions. The case records were taken consecutively from an alphabetical file of complete records—that is complete as to history, examination, and diagnosis.

TABLE 1

Analysis of 163 cases of headache

Type	No.	Localization	No.
Anterior	141	Ocular and Periocular	50
		Frontal	101
		Temple	27
		Combined	6
Posterior	52	Occipital	39
		Cervical	19
		Combined	6
Combined	30		

In looking over the cards it was seen that error would be introduced in several ways: (1) Inaccuracy of the patient in describing symptoms; (2) failure of the examiner to obtain a clear history; (3) inability of the examiner to arrive at a correct diagnosis; (4) absence of generally accepted standards for tabulating visual diagnoses.

The case histories were valuable because (1) each history was taken by the doctor personally (in a few instances they were begun by the secretary and completed by the doctor) and (2) the examinations were all done by the same person according to the same technique.

Certain arbitrary yardsticks were followed in determining diagnoses. For example, refractive error was not so classified without the presence of at least one prism diopter of spherical or astigmatic error. Presbyopia was taken as the point at which the total accommodation measured less than four and one-half diopters.

Of these 434 consecutive cases, 163 (37.5 percent) suffered from headaches alone, or from headaches in conjunction with other symptoms.

It seemed impracticable to separate primary and secondary headaches in a survey of this type. The 163 cards were searched for associated symptoms. Poor near vision and fatigue (asthenopia) were found most frequently associated with headaches. Subnormal vision came next and dizziness was fourth.

In tabulating the headaches, it was noted, as Moench had stated, that they tended to localize. They broke down into an anterior group, a posterior group, and a combination group. The anterior headaches were considered as those in front of a line drawn from ear to ear over the vertex.

The posterior headaches were considered as those lying behind this line. They were either occipital, posterior cervical, or both, and were found 52 times in the 163 cases.

The anterior cephalgias comprised frontal, periocular, and temple varieties. These were grouped together, and were found 141 times (Table 1).

Instances of combined anterior and posterior types occurred 30 times.

In an effort to determine whether there could be a correlation between diagnosis and localization, the two general types of headaches were separated, and the incidence of various diagnoses noted. Five etiologic factors stood out. They were refractive error, presbyopia, convergence insufficiency, convergence excess, and accommodative insufficiency (relative to the age). Again it was not possible to determine the primary and secondary diagnosis. So the diagnoses were simply tabulated, for frequency, as they occurred.

Several interesting things were noted concerning a correlation between diagnosis and localization: (1) Refractive error occurred about as frequently in one location as in another; (2) presbyopia was noted significantly more often in the posterior group than in the anterior group; (3) convergence

excess occurred more frequently in anterior headaches; (4) convergence insufficiency increased to a significant level in the posterior group (Table 2).

One is tempted to state that convergence insufficiency, with presbyopia, is prone to produce the posterior type of headache; whereas convergence excess tends to bring on an anterior type of cephalgia.

These figures are merely suggestive. There may be other associated factors not brought to light in this short and incomplete analysis. Definite conclusions should be based on a more detailed analysis of a greater number of cases.

TABLE 2

DIAGNOSES IN 163 CASES OF HEADACHE

Diagnosis	Anterior Headaches (141)		Posterior Headaches (52)	
	Instances Found	Percent	Instances Found	Percent
Refractive error	51	36%	17	33%
Anisometropia	4	2.8%	0	0
Presbyopia	37	26%	24	46%
Myopia (over 2.0D.)	1			
Hypermetropia (over 2.0D.)	3	2.1%		
Astigmatism (over 2.0D.)	4	2.8%		
Vertical imbalance	4	2.8%	1	
Lateral and vertical	1		1	
Convergence insufficiency	29	20%	25	49%
Convergence excess	41	29%	9	17%
Divergence excess	6	4%		
Accommodative insufficiency	28	19.9%	13	25%
Accommodative excess	9	6.4%	3	5.8%
Accommodative inequality	4	2.8%	1	

CAUSES OF OCULAR HEADACHES

It is not difficult to see the reason for the anterior type of headache in visual disability. The approximate anterior half of the upper cranium is supplied by the ophthalmic division of the fifth cranial nerve. If the endings of the nasociliary nerve are stimulated by prolonged or undue contraction of the ciliary muscles, referred pain is logically felt in the more superficial areas supplied by the frontal nerve. Because the nasociliary and frontal nerves are both branches of the ophthalmic division, pain may be referred from one nerve area to another without the excitation having traveled far, and without it having left the ophthalmic division of the fifth cranial nerve.

The manner in which a posterior type of headache can be produced from an eye stimulus is not easy to understand until one studies the central connections between the fifth cranial nerve and the upper three cervical nerves. Wolff shows by diagram this connection.[6]

Perelson[7] describes the anatomy as follows: "The descending tract of the trigeminal nerve descends through the pons and medulla to terminate as the spinal nucleus of the fifth nerve, which becomes continuous with the substantia gelatinosa of the upper cervical cord. The spinal tract of the fifth cranial nerve descends into the cervical spinal cord as far as the first and second cervical segments and may extend as far as the third cervical segment." The second and third cervical nerves enter the spinal cord via the tract of Lissauer to terminate in the substantia gelatinosa of the upper cervical cord where they synapse.[8]

Thus it can be seen how pain stimuli arising in the eye area supplied by the fifth

nerve, can spread posteriorly along the descending root of the trigeminal nerve to the upper three cervical cord segments, and by means of connections with the first three cervical nerves, set up referred pain in the area which they supply.

Kern[9] and Perelson,[7] in clinical studies, demonstrated how this connection can function by using cervical novocain injections. Kern gave relief to sufferers from cervical myositis, with referred anterior type headaches. Perelson found occipital nerve tenderness in a large number of patients suffering from widely varying forms of headache, including the anterior type.

It is quite within reason to feel that long-continued states of contracture of the extraocular muscles cause referred pain of the posterior type with secondary manifestations of hyperalgesia and muscle tenderness.

Determination of Headache

From a physiologic analysis of headache, it might seem that everyone should have cephalgia from a given stimulus. That this is not true, we are all aware. One patient may have severe headaches and another no pain at all, from the same aggravation. It will be necessary to analyze further the nature of pain and the human personality in order to understand why this is so.

The threshold of pain perceptions is about the same for all individuals at any time, and in any one individual at varying times.[10] The response to pain, however, varies from day to day, and greatly from one individual to another.[11]

This means that we all feel pain equally, but react differently. How we react depends on our emotional habits built up from past experiences, and on our present adjustment. Chapman[12] and his co-workers found that neurotic patients usually displayed a lower reaction threshold than normal individuals.

If one has two patients, each with the same degree of a given visual disability, one patient being calm and relaxed, the other under great emotional stress, the first will usually exhibit no headache, whereas, the second will likely show severe pain.

Summary

In a series of 434 patients from clinical practice, 37.5 percent with nonpathologic visual disabilities suffered from headaches.

These patients were grouped according to whether headache was localized anteriorly or posteriorly. There was suggestive correlation with certain diagnoses.

The reason why all patients do not develop headaches was discussed. The explanation suggested was that there is a variable response of the emotional pattern to a painful stimulus.

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MYOPIA, VITAMIN A, AND CALCIUM

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Among the numerous theories for the causation of myopia is the plausible one, from a clinical standpoint, of avitaminosis A and hypocalcemia. Investigators have given their views for or against these theories, but without laboratory studies to substantiate their opinions.

In this article 52 myopic patients and 20 hyperopic controls are reviewed clinically, as well as by laboratory studies, to show what role, if any, calcium and vitamins play in myopia.

Myopia is a variety of ametropia. It may progress to a certain stage and then gradually or suddenly stop increasing. Occasionally it may become malignant. When the myopia progresses still further, the myopic eye may develop a pathologic condition, with permanent visual detriment.

Sourasky[1] divided his myopia cases into low (up to −3.0D.); medium (up to −6.0D.); and high (above −6.0D.).

Tschernig and others suggested that eyes with a myopia over −9.0D. be designated as malignant.

A number of suggestions for the cause of myopia have been given, and have been reviewed by Rodin,[2] Prangen,[3] Burton,[4] Stansburg,[5] and others.

To illustrate how the different types of ametropia, as compared with myopia, progress over a number of years, several hundred cases from my records are here reviewed. They were unselected except in that each record had to show at least two separate refractions (ordinarily there was an interval of at least two years between refractions). Some records had as many as 10 or more refractions and covered a period of 25 years or more.

Review of over 300 cases of ametropia

Hyperopia

There were 25 patients in this group. A few of these patients were refracted as many as five times. Only slight differences were shown in each succeeding refraction. Usually a quarter up to a diopter increase was observed between the very first and the last refraction. Occasionally a slight decrease in refraction was noted. The maximum increase of 1.5D. of hyperopia was seen in only two patients. This covered a period of six years (three examinations) in one case, and 17 years (four examinations) in the other. Ten patients showed no progress of the hyperopia within periods ranging from 2 to 11 years.

Hyperopic astigmatism

There were 101 cases of this type of ametropia. One of these patients was under observation for 28 years.

There were 22 patients who, when they were first examined, had an age range up to 19 years. This includes the age of puberty, which Henderson[6] claims is about the time at which the eye is fully developed. They were reëxamined from 2 to 4 times over a period up to 15 years. They never gave an increase of more than a half of a diopter between the first and the last refraction. In fact, eight patients lost some of their hyperopia, and six children showed no change whatever in their succeeding refractions.

In the remainder of this group, the greatest change observed between the first and the last refraction, in one case only, was 1.75D. In one patient the difference between the first and the last refraction, done 23 years later, was one diopter in one eye, and a quarter of a diopter in the other. In a few old persons, the hyperopia decreased; in these cases there were some associated lenticular changes.

Miscellaneous cases

Anisometropia and mixed astigmatism. There were 17 cases in this group. They were examined between 2 and 4 times and

over a period of 18 years. Only one case of mixed astigmatism showed a total difference of one diopter between the first examination and the last one, 15 years later. The balance showed almost the same refraction, or, at most, a three-quarter diopter difference between the first and the last refraction.

Myopia

In this group there were 28 cases; unfortunately, a few were adults on their first examination, so that, being past puberty, they did not show the increase in their myopia as would be expected. Sixteen children were reëxamined up to four times and over a period of eight years (table 1). In all, the myopia had increased to a marked degree as compared with individuals showing hyperopia and hyperopic astigmatism.

Table 1 illustrates the varied progress of myopia in a few patients in this group.

Simple and compound myopic astigmatism

There were 124 cases in this group. Less than one half of the patients were under 19 years of age.

The progress of the myopia varied. Eight children showed no increase in myopia over a two-year period; five, an increase of 1.25D., four, a myopic increase bordering on malignancy (−9.0D.). These last four patients have showed no appreciable increase in their myopia within the last five years; their vision is normal.

Table 2 shows the varied progress of the myopia in this group.

Astigmatism developing in myopia on succeeding refractions

A significant, although small, group was this one of 25 patients. Here one observed the different varieties of progress encountered in all types of ametropia. Several cases showed no progress whatever, while in the remaining number, the increase in myopia ranged from −1.0D. to, in the extreme case, over −5.0D. in 12 years (table 3). The acquisition of an astigmatism in a case of myopia in children, did not lead to a cessation of the progress of myopia; often both the myopia and the astigmatism increased up to the beginning of the third decade of life.

Table 3 shows astigmatism developing in myopic patients after a previous myopic refraction.

TABLE 1

Cases of myopia*

Cases	Age at 1st Examination	Duration—1st to Last Refraction	Showed Increase of Myopia	
			O.D.	O.S.
	(years)	(years)	(D. sph.)	(D. sph.)
1. D. R.	9	1	−1.50	−0.75
2. E. G.	12	7	−2.25	−1.50
3. D. H.†	8	8	−3.25	−3.00
4. B. L.‡	7	7	−3.75	−4.25
5. L. L.	6	2	−3.75	−4.25
6. P. L.	13	3	−0.25	−1.62

* In all these cases, a small cylinder, if present, is omitted.
† For the last four years, there was no increase in the myopia.
‡ A brother has a mild nonprogressive myopia.

Other observations in the review of cases

Hyperopia developing into myopia

There were eight children with a low

TABLE 2

SIMPLE AND COMPOUND MYOPIC ASTIGMATISM

Case	Age at 1st Examination	Duration between 1st and Last Refraction	Showed an Increase of Myopia	
			O.D.	O.S.
	(years)	(years)	(D. sph.)	(D. sph.)
1. B. L.	12	4	−1.50	−1.75
2. J. L.*	14	3	none	−0.25
3. L. L.*	12	2	−0.75	−0.75
4. B. K.	10	3	−2.00	−2.25
5. L. K.	13	3	−1.50	−2.00
6. R. A.†	17	9	−3.75	−3.75
7. S. F.	8	2	−1.12	−1.50

* J. L. and L. L. are sisters. The father is also myopic.
† R. A., a medical student, original vision was:
O.D., −0.75D. sph. −0.5D. cyl. ax. 90° = 6/6
O.S., −0.75D. sph. −0.25D. cyl. ax. 90° = 6/6
His present refraction is:
O.D., −4.5D. sph. −0.5D. cyl. ax. 40° = 6/6
O.S., −4.5D. sph. −0.25D. cyl. ax. 60° = 6/6 !
Since he is now aged 26 years, there is little chance of excessive increase of his myopia.

TABLE 3

ASTIGMATISM DEVELOPING IN MYOPIA

Case*	Age at 1st Examination	Duration between 1st and Last Refractions	Increase in Myopia and Astigmatism between the 1st and Last Refractions	
	(years)	(years)	(sphere)	(cylinder)
1. S. L.	11	23	O.D. −2.25	−0.50
			O.S. −0.75	none
2. R. K.	10	17	O.D. −2.00	−0.50
			O.S. −3.00	−0.25
3. M. L.	13	4	O.D. −2.00	−0.75
			O.S. −1.75	−1.25
4. E. L.	10	17	O.D. −1.75	none
			O.S. −2.00	−1.00
5. N. L.	8	8	O.D. −3.00	−2.00
			O.S. −4.50	−1.75
6. R. G.	10	11	O.D. −1.50	−0.75
			O.S. −2.25	−0.37
7. M. G.	11	8	O.D. −2.25	−0.25
			O.S. −2.00	−0.25
8. M. I.	9	12	O.D. −5.25	−0.75
			O.S. −5.25	−0.50

* In Cases 1, 4, 5, and 8, members of the immediate family also had myopia.

degree of hyperopia who later developed myopia, a condition to which de Schweinitz[7] previously called attention.

MALNUTRITION

A few of the myopic children showed evidence either of previous or present malnu-

trition. However, this condition was also observed in some of the hyperopic children. One finds it difficult to associate myopia with poor eating habits as does Miller.[8]

Heredity

Unquestionably heredity does account for a considerable number of cases of myopia, as has been observed in some of the cases herein reviewed. An outstanding example were three brothers. Their father was myopic. All had axial myopia of between −5.0 to −6.0 diopters; their myopic progress stopped, as in most myopes, before the beginning of the third decade of life. Other than the ordinary diseases of childhood, they all enjoyed good health, and all were athletically inclined.

Avitaminosis and Hypocalcemia as causes of myopia

A number of observers have given clinical evidence of the association between hypocalcemia, avitaminosis A, and the progress of myopia. Among these are Walker,[9] Laws,[10] A. A. Knapp,[11] and Sathaye.[12]

Possibly the most interesting clinical report on the value of calcium is that of Strebel.[13] He claimed that the sclera contains about three percent of calcium. He reviewed the record of several of his patients in whom there was either an emmetropia or a mild hyperopia. Two of these patients, wives of physicians, became pregnant at the age of 30 years, and, as a complication, showed an associated hypocalcemia with the usual loss of teeth and the falling out of tooth fillings. His cases were interesting, however, in that, associated with the tooth decay, there developed a myopia. The development of myopia in an adult is an extremely rare complication.

Impressed by Strebel's report, I treated 20 patients for over a year with vitamins and calcium, and did frequent ophthalmic examinations. However, I did no laboratory studies to determine a definite hypocalcemia in these myopic cases which were studied but the results appeared interesting enough to warrant further investigation.

Both the proponents of the theory of vitamin-A and calcium deficiencies as a cause of myopia and Laval,[14] Corvan,[15] and Cowan,[16] who opposed this theory, omitted laboratory studies to substantiate their individual claims. At the time of their reports, the tests were not easily available; besides they are painstaking, time consuming, and relatively expensive.

Laboratory studies

To determine the role of calcium and vitamin A in myopia, 52 myopes were studied (table 4); 20 hyperopes acted as controls. Each myopic patient was refracted under atropine and given full correction according to the suggestion of Duane,[17] with directions for continuous wearing of glasses as advised by Jackson.[18]

Included in the myopic group were several progressive myopes, already under my care, and a few adults who were at the age when one would expect the calcium balance to be stabilized. Each patient received a laboratory study including total calcium, bound, percentage diffusible, and ionic calcium (ca++); vitamin A, beta carotene, protein, inorganic phosphorus, and dark adaptation.[19]

Immediately after the laboratory tests were completed, the vitamins and minerals were given to these patients in potent dosages. The multiple vitamins were used because it is claimed that their combined rather than individual use is most beneficial. The addition of minerals was employed because deficiencies in diet often include minerals as well as vitamins. It is claimed that the same processes in the body extract both vitamins and minerals. The patients were reëxamined every 3 to 4 months, and medication was adjusted to the progress of the myopia.

TABLE 4

LABORATORY RECORDS OF THE PATIENTS RECEIVING LABORATORY STUDIES

Case No.	Name	Age	Sex	Total	Calcium		% Diff.	Vitamin A	Beta Carotene	Protein	Ing. Phos.	Blood Sugar	Hanger		Dark Adapt.	
					Ionic*	Bound							24	48		
					(Ca++)			(Gamma)	(Gamma)				(hours)		(min.)	(sec.)
1	I. A.	50	F	10.3	4.8	5.5	46.6	34	70	6.9	3.55				2	17
2	M. B.	22	F	10.2	5.2	5.0	51.0	38	72	6.3	3.4					
3	A. B.	8	F	10.6	5.6	5.0	53.0			6.68	4.5	98	Neg.			
	2nd Exam.—			10.9	5.8	5.1	53.2	24	48	7.35	4.8				3	
4	R. B.	47	F	9.0	4.0	5.0	44.4	28	56	6.15	2.4					
5	S. B.	10	F	9.8	4.6	5.2	46.9	30	62	6.41	4.3				5	
6	H. B.	12	F	9.8	4.4	5.4	44.9			6.4	4.15	78	+1	+2		
7	F. C.	17	F	10.3	4.8	5.5	45.6	36	72	6.0	3.7					
8	R. C.	29	F	10.4	4.7	5.7	45.1	40	80	6.65	2.6					
9	B. C.	14	M	11.0	5.0	6.0	45.5	42	84	6.5	4.3					
10	R. D.	8	M	11.0	5.2	5.8	47.2	36	72	6.1	4.7					
11	A. G.	10	F	9.7	4.6	5.1	47.0	80	162	6.22	4.5				3	30
12	B. G.	11	F	10.3	5.0	5.3	48.5	34	56	6.75	4.15				6	30
13	H. G.	9	M	10.2	4.9	5.3	48.4	66	88	6.58	3.2					
14	T. H.	57	M	10.4	5.4	5.0	51.9	56	114	6.52	3.4					
15	N. H.	14	M	10.2	4.6	5.6	45.0	32	64	5.81	5.75					
16	G. J.	7	M	9.3	5.2	4.1	56.0	115	236	6.08	4.5				6	14
17	J. J.	14	M	11.3	5.8	5.5	51.3	72	148	6.8	3.65					
18	M. J.	8	F	10.9	5.5	5.4	50.4	50	104	7.2	5.00					
19	R. J.	8	M	9.9	4.6	5.3	46.4	68	135	6.0	3.7				5	
20	A. K.	5	M	10.6	4.8	5.8	45.2	24	48	6.55	5.15				4	
21	T. K.	10	F	10.0	4.5	5.5	45.0			6.35	4.7		−	+1		
22	L. K.	8	F	10.4	4.2	6.2	40.3			7.25	4.15	109	Neg.			
23	A. K.	14	M	10.2	5.1	5.1	50.0	42	92	6.60	3.6				4	2
24	S. K.	57	F	9.8	4.5	5.3	45.5	94	185	6.82	3.5				3	20
25	L. L.	6	F	9.6	4.0	5.6	41.6	85	170	6.08	4.8	98	Neg.		10	
	2nd Exam.—			14.2	7.4	6.8	52.0			6.15	4.7					
26	J. L.	7	F	11.0	4.8	7.2	43.6	56	109	6.55	4.8				3	32
27	P. L.	8	M	10.0	6.0	4.0	60.0	64	128	7.25	2.3					
28	M. L.	4	M	10.8	4.6	6.2	42.6	30	60	5.82	4.9					
29	J. M.	9	F	10.2	4.0	6.2	39.2			7.35	3.8	109		+1		
30	S. M.	9	F	10.5	4.8	5.7	45.7			6.5	4.4	106	−			
	2nd Exam.—			9.4						6.2	4.75				7	15
	3rd Exam.—			9.4	4.4	5.0	46.8	22	40	6.2	4.75					
31	A. M.	15	M	9.5	4.1	5.4	43.1	33	66	6.30	3.9					
32	B. M.	7	F	9.0	4.2	4.8	46.0	27	53	6.85	3.4				6	20
33	B. M.	10	F	10.2	5.0	5.2	50.0	33	62	6.15	3.6				3	
34	B. O.	3	F	8.7	3.7	5.0	42.3			6.35	3.9	113	Neg.			
35	S. P.	7	F	9.4	4.3	5.1	45.7	32	64	6.4	4.3					
36	R. R.	25	M	9.0	4.1	4.9	45.5	88	170	6.60	2.95				45	
37	R. S.	32	F	9.1	4.6	4.5	50.5	42	82	7.2	1.9				2	30
38	J. S.	8	M	10.5	4.2	6.3	40.0	62	124	6.65	4.5				3	14
39	J. S.	38	M	9.0	4.2	4.8	46.4	34	66	6.4	2.7				8	40
40	P. S.	13	M	9.4	4.6	4.8	49.0	52	104	6.58	3.1					
41	S. S.	10	F	10.0	4.6	4.8	48.0			6.0	5.0	95	−	+1		
42	C. S.		F	10.9	5.2	5.7	47.7	34	68	6.12	4.3				4	14
43	J. T.	12	M	10.5	4.6	5.9	43.8			6.52	4.7	126	Neg.			
44	M. T.	11	M	10.0	5.3	4.7	53.0	60	120	6.15	3.4					
45	D. W.	20	M	10.8	5.0	5.8	46.0	48		6.4	4.9					
46	S. W.	8	M	8.6	4.0	4.6	46.5	30	62	5.8	5.1				2	53
47	D. W.	13	M	9.8	4.2	5.6	43.8			6.85	4.7	98	+1	+1		
48	B. W.	16	F	11.0	5.2	5.8	47.2	48	96	7.2	2.8				8	
49	L. W.	26	F	9.0	3.8	5.2	42.2	28	54	5.68	2.5				7	3
50	L. Z.	9	M	8.3	3.3	5.0		33	62	5.72	5.0					
	2nd Exam.—			10.1	4.5	5.6	44.5			7.05	3.9	106	Neg.			

* Ionic calcium was determined after the method of McLean and Hastings.[30]

If necessary, it was augmented by increasing the vitamin A or calcium and by adding phosphorus, vitamin D, and, in a severe case, a very potent medication, dihydrotachysterol (T10). In this severe case, the mother of the patient was shown how to do the Sulkowitch test of the urine, so as to detect an oncoming hypercalcemia.

The study was continued for about two years. A few patients had two blood studies; one was rechecked three times. The ages of the patients ranged from 3 to 57 years.

REVIEW OF THE PATIENTS TAKING THE LABORATORY TESTS*

The blood studies of the first 23 patients showed all to be normal for vitamin A and beta carotene. Nine, however, showed a pathologic dark adaptation. On being questioned, four of these said that they were fully aware that they were night blind.

It is known that myopes often show a pathologic dark adaptation; this, however,

* I am indebted to A. Steinberg, B.S., and to Dr. H. Segal for aiding in the laboratory studies.

is not due to avitaminosis A, but rather to an anatomic defect caused possibly by the distortion of the rods, as would occur in axial myopia. Attention to this type of pathologic dark adaptation has been previously mentioned by me.[21]

After the first 23 cases, blood sugar and Hanger tests (cephalin-cholesterol-flocculation) were substituted for the vitamin-A and carotene studies.

It is possible that the increase in myopia following stoppage of vitamin A and calcium was purely coincidental.

Case 26. J. L., whose mother was highly myopic, was aged seven years, when first seen in 1942. Her correction was: O.D., −3.25D. sph. ⊂ −1.0D. cyl. ax. 180° = 6/6; O.S., −4.25D. sph. = 6/6. Her myopia had increased by a diopter every year, regardless of vitamins and calcium which, as in Case 10, were not prescribed by a physician. The laboratory studies showed only a slightly lower percentage differential calcium.

Her present correction is: O.D., −9.0D. sph. ⊂ −1.25D. cyl. ax. 180° = 6/9 + 4; O.S., −11.0D. sph. = 6/9 + 4. Little benefit was gained by the vitamin-A and calcium therapy.

Case 27. P. L., a medical student, whose father was also myopic, was eight years of age when I first examined him in 1927. His original correction was: O.D., −1.0D. sph. = 6/6; O.S., −0.5D. sph. = 6/6. He never took any vitamins or calcium. Although myopic he had an unusually high ionic calcium (ca++), even more than any of the control hyperopic cases. His low phosphorus was only exceeded by Case 37 who also had a normal calcium. In spite of the constant use of his eyes and lack of exercise, his myopia, although increasing is not of the high myopic type. At his present age of 30 years, there is little likelihood that there will be much increase in the myopia.

Case 30. S. M., aged nine years, had no history of myopia in her family. Her laboratory studies showed a decrease in the percentage differential

TABLE 5

LABORATORY RECORDS OF HYPEROPIC PATIENTS RECEIVING LABORATORY STUDIES AS CONTROL CASES

Case No.	Name	Age	Sex	Calcium				Protein	Ing. Phos.	Blood Sugar	Hanger	
				Total	Ionic	Bound	% Diff.				24	48
					(Ca++)						(hours)	
1	S. A.	3	M	8.4	3.8	4.2	45.2	6.05	4.8	85	+1	+2
2	N. B.	11	F	10.5	5.2	5.3	50.0	7.1	4.3	100		Neg.
3	R. B.	5	M	10.5	4.6	4.9	53.3	6.51	4.5	95	−	+1
4	M. B.	4	F	10.6	5.2	5.4	49.0	6.9	3.9	87	+1	+2
5	J. B.	10	M	10.0	4.2	5.6	42.0	6.30	4.0	122	+1	
6	N. E.	6	F	9.3	3.9	5.4	42.0	6.50	4.6	94		Neg.
7	M. F.	2	F	10.3	4.9	5.4	47.4	6.42	4.4	86	+1	+1
8	B. F.	3	F	10.4	5.9	5.9	43.2	7.0	5.0	106	+4	+4
9	N. G.	1	F	9.6	4.8	4.8	50.0	6.9	5.0	106		Neg.
10	H. H.	2	M	9.8	5.0	4.8	51.0	6.15	4.8	98		Neg.
11	C. H.	5	F	13.6	6.8	6.8	50.0	6.5	4.7	100	+1	
12	C. K.	2	F	9.6	4.2	5.4	43.7	6.85	4.2	113	−	+1
13	B. K.	4	F	10.2	4.5	5.7	44.1	6.85	5.2	103.5	−	+1
14	S. L.	5	F	9.6	4.3	5.3	44.8	6.0	4.5	92	−	+1
15	C. L.	1	F	10.1	4.0	6.1	39.6	6.15	5.3	86	+1	+2
16	S. M.	2	F	11.0	5.5	5.5	50.0	6.52	4.55	100	−	Neg.
17	M. M.	4	M	9.04	4.0	5.04	44.4	5.9	4.80	95		Neg.
18	B. P.	4	M	10.7	5.1	4.6	47.6	6.1	5.1	121		Neg.
19	S. R.	6	M	9.60	4.5	5.1	47.0	6.25	4.15	116		Neg.
20	D. U.	4	M	10.4	5.5	5.4	50.4	6.15	4.5	95	−	+1

CLINICAL CASES (table 4)

Because of the interesting phenomenon observed, a few of the 52 cases that obtained laboratory studies are here discussed.

Case 10. R. D., aged 8 years, first saw me in 1942. His myopia was −2.25D. sph. and was gradually increasing. In December, 1947, laboratory studies were done and showed a slight diminution of the percentage differential calcium, despite the fact that he had taken vitamins and minerals for five years. The other laboratory studies were negative. Since the vitamins and minerals were not ordered by a physician, and because his myopia had not increased for nine months, they were discontinued.

Several months following this, the myopia showed an increase of −1.0D. His correction was now: O.D., −6.0D. sph. = 6/6; O.S., −5.5D. sph. = 6/6.

calcium. She has been taking high potency calcium, and vitamins, augmented at times by phosphorus, vitamin D, and even dihydrotachysterol (T10). In spite of the medication used, myopia in her left eye has increased −1.75D. within eight months. She is now slightly over 11 years of age and her correction is: O.D., −7.75D. sph. ⌒ −0.25D. cyl. ax. 90° = 6/9; O.S., −9.75D. sph. = 6/9.

Calcium and vitamin therapy did not affect the myopia in this case.

Case 41. The case of S. S. is interesting in that it possibly shows the value of attempting to correct associated disorders in the management of myopia as would be done in other diseases of long standing without known cause.

This patient was 10 years of age and, when first seen, had a hypothyroid condition. She had taken vitamins and minerals ordered by her physician long before I saw her in 1946. Her myopia increased −2.0D. in both eyes in two years, even though I prescribed massive doses of vitamins, calcium, and phosphorus. Her last basal metabolism rate, after taking thyroid extract for nine months, was −16; an improvement over the previous basal metabolism rate of −25. During these nine months her vision remained stationary. Whether this is coincidental or not, it is impossible to say at the present time, but it may be that the myopia improved with the correction of the thyroid condition

Case 49. L. W., aged 26 years, was pregnant. She had a low ionic calcium, percentage differential calcium, and inorganic phosphorus. She was myopic and in spite of her laboratory study and my suggestion that calcium and vitamins be taken, and particularly on account of her pregnancy, she omitted taking them. Her myopia remained the same over the two-year period of study, including the pregnancy.

Case 50. L. Z., aged nine years, had two blood studies. His father is myopic, but his two brothers are not. His first test showed a slightly diminished total, ionic, and percentage differential calcium which was improved on his second test nine months later. Nevertheless, in spite of the improvement in the laboratory study, his myopia had increased 1.75D., in the right eye, and 3.0D., in the left eye. All this regardless of the fact that he had continuously used vitamins and calcium.

Control cases (table 5)

Among the 20 hyperopes who acted as controls, total calcium was slightly less in one patient; ionic calcium was less in four patients; in 13, the percentage differential calcium was subnormal.

Blood sugar and Hanger tests

The blood sugars of both hyperopes and myopes were within normal limits. The Hanger test showed a pathologic condition in one case, M. F., a hyperope (table 4).

The two hyperopes did not show a hypocalcemia by laboratory study when they changed to myopia (table 6).

TABLE 6

Laboratory findings in two cases of hyperopia which changed to myopia

Case No.	Name	Age	Sex	Total	Calcium		% Diff.	Vitamin A	Beta Carotene	Protein	Ing. Phos.	Blood Sugar	Hanger		Dark Adapt.	
					Ionic*	Bound							24	48		
					(Ca++)			(Gamma)	(Gamma)				(hours)		(min.)	(sec.)
1	N. D.	9	M	9.2	4.2	5.0	45.6	38	76	5.62	4.9					
2	B. D.	9	F	10.1	5.0	5.1	46	36	72	6.32	3.75				6	

* Ionic calcium was determined after the method of McLean and Hastings.[29]

Conclusion

Myopia is the most progressive of all types of ametropia.

Myopia may increase slowly, rapidly, or stop progressing suddenly. The most activity in the progress of myopia is seen up to or about the middle of the second decade of life.

Malignant myopia (over −9.0D.) is not very common. Among the first group of over 300 cases of ametropia discussed herein, only four patients had a refraction of over −9.0D. Only two of the 52 myopes who obtained laboratory studies had malignant myopia.

Laboratory tests on the 52 myopic cases showed:

Three patients (6 percent) had a slightly less than normal total calcium.

Three patients (6 percent) had a slightly less than normal ionic (ca++) calcium.

Forty patients (77 percent) had a subnormal percentage differential calcium.

The 20 hyperopes who acted as controls showed: One patient (5 percent) had a low total calcium. Four patients (20 percent) had subnormal ionic (ca_{++}) calcium.

Eleven patients (55 percent) had a low percentage differential calcium.

It is possible that some myopes felt that their vision was improved by the taking of vitamins or minerals; however, their improvement was not verified by corroborative laboratory studies, nor were such cases observed over a long period of time.

Possibly the ideal treatment for myopia, in view of the fact that the exact etiology is not known, would be, as in all chronic conditions of unknown origin, to correct any deficiency present, such as avitaminosis or glandular disorder, and to investigate and treat any focus of infection.

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Ophthalmic Miniature

How often too, do we not have to treat different ocular diseases coming from the same origin (syphilis): notably a particular kind of cold ophthalmia with obscuring of vision!

Johannis de Vigo, Liber Quintus: *De Morbo Gallico*, 1534.

ALBINISM*

Report of an unusual family

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Albinism is not a rare condition. It has been observed by numerous investigators from the time of Hippocrates to the present. Three albinos and their normally pigmented brother are being presented here because of several features that seem worthy of emphasis: (1) The high ratio of albino to normal siblings; (2) the high intelligence of the albinos; and (3) the occurrence of identical central nervous-system anomalies in the three albinos.

The first two observations have been made previously by other observers. Although albinism with co-existing central nervous-system anomalies has been noted, albinism associated with identical central nervous-system anomalies in siblings has not been reported.

The ancestors of the subjects of this discussion, as far back as the great grandparents, were known to be normally pigmented, and no intermarriage had occurred in these three generations. The first of the mother's five pregnancies terminated in a spontaneous abortion. Three of the children were complete albinos; the fourth was normally pigmented.

Each sibling was given a complete physical examination. Special attention was given the nervous system, including the vestibular and auditory systems and the visual apparatus. Color perception was tested on pseudo-isochromatic plates.† Intelligence was estimated by the Wechsler-Bellevue test.

Case reports

Case 1

R. C., a young man, aged 20 years, attending college, was a complete albino.

Physical examination, including a careful neurological examination, revealed no abnormalities except the albinism and its accompanying amblyopia and nystagmus. Side-to-side head movements were sometimes present.

Eye examination. The uncorrected visual acuity for each eye was 20/200. The near vision was: O.D., J11 at 14 inches and J4 at four inches; O.S., J10 at 14 inches and J3 at four and one-half inches.

A horizontal ocular nystagmus was present, and this increased markedly on gazing to the left. The nystagmus was plainly evident when the eyes were closed. The irides were pale gray. The pupils were equal and reacted promptly to light and to convergence.

There were 6.0 p.d. of esophoria at 20 feet and 3.0 p.d. of exophoria at 14 inches. There were 8.0 p.d. of left hyperphoria at 20 feet and 4.0 p.d. of left hyperphoria at 14 inches. There was no diplopia. No anomalies were detected by slitlamp examination.

Ophthalmoscopy, including examination in red-free light, failed to reveal a macula or retinal pigment.

Retinoscopy and refraction under homatropine cycloplegia showed a refractive error: O.D., −2.0D. sph. ⊂ +3.0D. cyl. ax. 105°, with vision of 20/200; O.S., −1.5D. sph. ⊂ +1.5D. cyl. ax. 90°, with vision of 20/100.

Color perception was normal. The audiogram showed normal hearing. The caloric test, using ice water, resulted in vertigo but was difficult to evaluate objectively because of the nystagmus already present.

The verbal score on the Wechsler-Bellevue intelligence test was 146 or very superior, and the performance score was 109, or average. This represents a drop of 25 percent. In spite of this relatively low performance score, however, the total of 131 is still in the very superior range and places him in the upper one percent of the population.

Case 2

W. C., a boy in high school, aged 18 years, was a complete albino. No physical abnormalities other than the albinism and the ocular anomalies were detected. Side-to-side head movements were not present.

Eye examination. The uncorrected visual acuity

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* From the Birmingham Veterans Administration Hospital. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

† American Optical Company.

was: O.D., 20/400, J11 at 14 inches and J4 at three and one-half inches; O.S., 20/200+1, J11 at 14 inches and J3 at three and one-half inches.

Retinoscopy and refraction under homatropine cycloplegia revealed a refractive error: O.D., −0.5D. sph. ⊃ +3.5D. cyl. ax. 90°, with vision of 20/200; O.S., +3.0D. cyl. ax. 90°, with vision of 20/100.

A horizontal ocular nystagmus was present and increased on gazing to the left. The nystagmus was plainly evident when the eyes were closed. The irides were pale gray. The pupils were equal and reacted promptly to light and to convergence. Remnants of the pupillary membrane were presented bilaterally: O.D., from the 4:30- to 5-o'clock positions; O.S., from the 4:30- to 7-o'clock positions. A healed small round corneal macular opacity was present in the center of the left cornea.

Ophthalmoscopy, including examination in red-free light, revealed no evidence of a macula. In the posterior pole of each eye an area of the fundus appeared darker than the rest. This occupied an area of about four disc diameters and was thought to represent pigment.

There were 6.0 p.d. of esophoria at 20 feet and 4.0 p.d. of exophoria at 14 inches. There were 4.0 p.d. of left hyperphoria at 20 feet and 6.0 p.d. of left hyperphoria at 14 inches. There was no diplopia.

Color perception was normal. The audiogram showed normal hearing. Caloric test using ice water resulted in subjective vertigo and nausea.

The verbal score on the Wechsler-Bellevue intelligence test was 130, or very superior, and the performance score was 96, or average. This represents a drop of 34 percent. The total of 117 places him in the bright normal range, or in the upper 11 percent of the population.

Case 3

J. C., a girl, aged 9 years and 10 months, was a complete albino. Side-to-side head movements were sometimes present.

Eye examination. The uncorrected visual acuity was: O.D., 20/200, J11 at 14 inches and J3 at four inches; O.S., 20/200, J11 at 14 inches and J2 at four inches.

A horizontal ocular nystagmus was present and was somewhat more marked on gazing to the left. The nystagmus was plainly evident when the eyes were closed. The irides were pale gray. The pupils reacted promptly to light and to convergence. There was 1.0 p.d. of left hyperphoria at 20 feet and 1.0 p.d. of left hyperphoria at 14 inches. There were 5.0 p.d. of exophoria at 20 feet and 9.0 p.d. of exophoria at 14 inches. The exophoria alternated with an exotropia at both near and distance. This measured 30 degrees on the perimeter and was most marked at the near point. No anomalies were detected by slitlamp examination.

Ophthalmoscopy, including examination in red-free light failed to reveal a macula or retinal pigment.

Refraction revealed a manifest error of: O.D., +2.0D. cyl. ax. 90°, with vision of 20/200; O.S., −0.5D. sph. ⊃ +1.25D. cyl. ax. 105°, with vision of 20/200.

Color perception was normal. The audiogram showed normal hearing. A caloric test was not performed as the subject had had motion sickness on the morning of examination.

The verbal score on the Wechsler-Bellevue intelligence test was 117, or in the bright normal range, while the performance score was 108, or average. The drop in this case was only eight percent. The total of 113 places her in the bright normal range, or in the upper 20 percent. These scores may have been influenced by the fact that the subject had had nausea and vomiting just before the administration of the test.

Case 4

W. C., a boy in high school, aged 17 years, was a normally pigmented, blond, blue-eyed individual. Physical examination revealed no abnormalities.

Eye examination. The uncorrected visual acuity was: O.D., 20/15—1 and J1 at 14 inches; O.S., 20/15 and J1 at 14 inches. Pupils were equal and reacted to light and to convergence. There were 2.0 p.d. of esophoria at 20 feet and 7.0 p.d. of exophoria at 14 inches. There was 0.5 p.d. of left hyperphoria at 20 feet and 1.0 p.d. of left hyperphoria at 14 inches.

There was no nystagmus and no diplopia. The fundus pigment was normal and the macular reflex and macular pigment were present. Refraction revealed a manifest error of: O.D., +0.5D. cyl. ax. 180°, vision 20/15; O.S. +0.25D. sph. ⊃ +0.5D. cyl. ax. 180°, vision 20/15.

Color perception was normal. The audiogram showed normal hearing.

The verbal score on the Wechsler-Bellevue intelligence test was 128, or very superior, while the performance score was 116, or in the bright normal range. This represents a drop of nine percent. The total score was 126, or superior, placing him in the upper three percent of the population.

Comment

None of the three albinos showed evidence of a macula. One had a congenital anomaly of the eyes other than albinism (remnant of pupillary membrane). All showed evidence of an anomaly of the central nervous system in that the nystagmus increased in arc and in rate on gazing to the left and decreased somewhat on gazing to the right.

Since there was no evidence for paralysis of a horizontally acting muscle, especially since Case 3 had an alternating exophoria and exotropia, it was felt that there must be

an incomplete conjugate paralysis of the coordinated movements of the eyes. Each of the four individuals was right handed, and each was subject to motion sickness.

It was striking that each of the albinos preferred the left eye, and that there was a left hyperphoria in all four subjects. This was marked in two of the albinos. Three of the subjects had an esophoria for distance, while one of the albinos had an alternating exophoria and exotropia. The refractive errors of the albinos did not fall into a pattern. The predominant component was hyperopic astigmatism.

Discussion

It is commonly stated that albinism is inherited as a simple recessive factor,[1] and, certainly, numerous instances have been collected in which this seems to have been the mode of inheritance.[2, 3] Contrary observations have also been made. Davenport and Davenport[3] included in their series a family in which 3 of 5 siblings of normally pigmented parents were albino; a family in which 6 of 9 siblings of normally pigmented parents were albino; and a family in which 8 of 9 siblings of normally pigmented parents were albino.

Elschnig[4] presented a family in which a normally pigmented couple had three children, all albino. Bateson[5] stated that Magnus found a normally pigmented couple with one normally pigmented and seven albino children. Weber[6] reported a family in which 6 of 13 children of normally pigmented parents were albino.

Although in our cases, there was no history of albinism in any ancestors, albinism occurred in 75 percent instead of the expected 25 percent of the progeny. This ratio does not include the fetus lost by spontaneous abortion. It is possible, that had there been more children, the ratio might have changed in favor of the normally pigmented individuals. Albinism was known not to have occurred in the ancestors as far back as the great grandparents. No intermarriages occurred in these three generations.

The Mendelian laws of inheritance are sometimes difficult to apply and, in such instances, Elschnig[4] suggested albinism as a disease or disturbance of the germ plasm. Fuchs[7] stated that, if albinos resulted from the progressive decrease of pigment, albinism should be more common in the northern, lightly pigmented races, and, since the opposite is true,[8] albinism must be considered a congenital anomaly.

Lack of development of the fovea centralis in albinotic eyes was demonstrated histologically in 1907 by Fritsch,[9] and was demonstrated in continuous serial sections in 1913 by Elschnig.[4]

The fovea of the human eye begins to develop at the end of the sixth fetal month, and after the eighth fetal month no further development is evident.[10] Elschnig[4] concludes that the development of the albino retina appears to have been arrested at an early stage. Manz,[11] in 1878, noted a minor anomaly in the "easy separation of the processus cornealis choroideae from the cornea" in an albinotic eye. He mentioned that anomalies associated with albinism, such as thinness of the sclera, persistence of the pupillary membrane, and delayed closure of the fetal ocular cleft had been pointed out by "other observers."

Gilbert,[12] in 1921, described the microscopic findings of an albino eye with reduplications of single retinal layers between the nervehead and the posterior pole. Apparently not aware of the statement by Manz, he suggested a relationship between albinism and other congenital anomalies of the eye.

Clark[13] reported absence of the sphincter muscle and partial aniridia, congenital pupillary membrane, atrophy of the disc, bilateral capsular cataract, and coloboma of the mesodermal tissue of the iris occurring in two cases of incomplete universal albinism. Persistence of remnants of the pupillary mem-

brane occurred in both eyes of one of our cases (case 2).

Thus it is apparent that albinism is associated not only with an arrest in the development of the retina alone, but frequently with other developmental arrests of the eye, both ectodermal and mesodermal.

Incomplete development of the retina is always found associated with albinism; other developmental anomalies of the eye occur less commonly. Two explanations are possible: (1) The development of the most highly differentiated structure, the retina, is most subject to disturbance, and (2) the differentiation of the retina occurs late in fetal development, thus leaving it vulnerable to influences occurring after other structures have attained comparative maturity.

That central nervous-system anomalies coexist with albinism has been recognized by Clark.[13] The presence of an identical central nervous-system anomaly in each of the three albinos described above, and its absence in their normally pigmented sibling, suggests an inherited common defect in the germ plasm, to which the albinism, the ocular anomalies, and the central nervous-system anomaly are secondary. The nature and origin of this defect remain obscure.

However, albinism has certain features in common with a group of conditions which have been termed congenital ectodermoses or neurocutaneous syndromes by Yakovlev and Guthrie.[14] The group includes: (1) Recklinghausen's neurofibromatosis, (2) Bourneville's tuberous sclerosis, and (3) angiomatosis of the brain with nevi of the skin in the trigeminal area. To these Wilcox[15] has added a fourth condition, melanomatosis of the skin and central nervous system.

These conditions are the result of congenital maldevelopment bearing chiefly on the organs of ectodermal derivation—nervous system, eyeball, retina, and skin. That the mesodermal structures (nevi) involved are closely associated with neuro-ectodermal tissues is evidenced by their distribution which corresponds with metameres or with areas of sympathetic innervation.

It is evident that albinism is similar to these conditions, although it differs from this group of conditions in several respects: (1) There is no metameric or sympathetic distribution; (2) manifestations of involvement of the central nervous system, especially epilepsy and feeble-mindedness which are prominent (although sometimes absent) in congenital ectodermoses, are inconspicuous in albinism (although associated feeble-mindedness or minor central nervous system anomalies sometimes occur); and (3) albinism is not confined to tissues of ectodermal origin, since at least in the eye the pigment of the iris and the choroid, generally considered of mesodermal origin, is deficient to a greater degree than the pigment of the retinal epithelium, which is of ectodermal origin. Associated developmental arrests may be ectodermal or mesodermal in type. However mesodermal involvement also occurs, although to a lesser extent, in the other conditions in this group.

Since these differences are mainly of degree, it is felt that albinism should be tentatively included in the group of congenital ectodermoses.

That albinism is not associated with mental deficiency has been shown by Beckham,[16] who interviewed and gave psychologic tests to 42 Negro albino children. The psychologic findings for the four cases of this report were striking enough to merit comment.

The two older albinos achieved performance scores that were 25 percent and 34 percent lower, respectively, than their verbal scores. The third albino showed a smaller drop (eight percent). This subject was much younger than the others, however, and because of emotional tension occasioned by motion sickness, the results in this case may be unreliable. The normally pigmented sibling showed a drop of nine percent in the performance score.

These results suggest that the defective

vision of the albinos retarded performance. The verbal scores of the two older albinos and of their normally pigmented sibling were in the very superior range. In spite of the low performance score, the oldest albino achieved a higher total score than his normally pigmented brother. The youngest albino achieved a verbal score and a total score in the bright normal range. It is apparent that in our subjects, albinism is not associated with mental deficiency.

Beckham[16] emphasized that "albinos have some definite problems, particularly those of family and personal adjustment," and that psychologic and psychiatric treatment are often necessary. Although, in our cases, psychologic testing was limited to estimation of intelligence, it was the impression of the psychologists, that the albinos tended to be shy and withdrawn as compared to their normally pigmented sibling.

Summary

1. Three albinos and their normally pigmented brother have been described.

2. The high ratio of albino to normally pigmented siblings has been considered in relation to Mendelian inheritance.

3. Identical central nervous-system anomalies in the three albinos have been described, and the possible significance of these anomalies in relation to the mode of inheritance has been discussed.

4. The similarity of albinism to such congenital ectodermoses as Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis, angiomatosis of the brain with nevi of the skin in the trigeminal area, and melanomatosis of the skin and central nervous system has been pointed out, and the inclusion of albinism with this group of conditions has been suggested.

5. The intelligence of each of the four siblings was estimated by the Wechsler-Bellevue test, and it was noted that the total scores achieved by the albino individuals compared favorably with the total score of their normally pigmented sibling. The scores ranged between the bright normal and the very superior levels, the highest score having been made by one of the albinos.

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The psychologic studies were done by Mrs. Gertrude Baker and Mr. David Ruja.

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NOTES, CASES, INSTRUMENTS

HERPES ZOSTER DISCIFORM KERATITIS*

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Keratitis disciformis is a localized, subacute, nonsuppurative, inflammation of the corneal parenchyma. It is chronic in nature and is characterized by a discoid opacity, epithelial edema and immense swelling of the deeper layers of the cornea. It is accompanied by symptoms of marked irritation, pain, photophobia, lacrimation, and circumcorneal injection. The entity was first described by Fuchs[1] in 1901.

Fig. 1 (Gaynon). Appearance of the right eye in a case of herpes zoster disciform keratitis.

The lesion may arise after trauma, herpes, vaccinia, varicella, syphilis, and exposure to hydrogen-sulfide gas. Cassuto[2] reported a case of bilateral keratitis disciformis following a croupous pneumonia.

The only case reported as having herpes zoster as a causative factor was that of Grandi.[3] In his paper, a soldier developed keratitis disciformis during the course of an ophthalmic herpes zoster.

CASE REPORT

History. J. S., a white man, aged 37 years, was first seen in May, 1946, complaining of diplopia of one day's duration. He had pain and tenderness over the right frontal area. He had been under treatment by his family physician for the past six days for herpes zoster of the right upper lid and forehead. No pathologic condition was demonstrable in the left eye.

Examination of the right eye. Vision was 20/15, J1. The typical ulcers and vesicle formation of herpes zoster were present along the distribution of the right frontal nerve. The lid was reddened, edematous, and some ptosis was present. The cornea was clear. The corneal reflex was diminished. Examination of the orbit revealed no pathologic process. The right external rectus muscle was completely paralyzed.

The patient was given a patch to wear and placed on heavy doses of vitamin-B complex.

Course. Upon his return, a month later, he stated that the paralysis had disappeared in a few days and that now within the past two days, the vision in the right eye had become blurred, the eye was red, painful, and there was much photophobia and tearing. The vision had dropped to 20/100.

On gross examination, the scars of the herpes of the lid were red. There was a marked circumcorneal congestion; the corneal surface appeared very uneven and hazy. The corneal reflex was absent. The cornea did not stain with fluorescein. Slitlamp examination showed the surface of the cornea to be hazy and rough. There was marked interstitial haze in the deeper layers of the parenchyma and a marked central thickening of the cornea was evidenced by the marked annular reflex. Almost the entire cornea was involved.

The patient was placed on atropine, penicillin, and vitamin-A and D ointment locally. The process began to resolve. There was less redness, the limbal portions of the cornea began to clear, and the vision through the dilated pupil increased to 20/50.

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During the following July, more pain and congestion developed in the same eye. Two small superficial punctate ulcers were found at the apex of the cornea. The ulcers healed within a few days. The congestion gradually disappeared, the corneal epithelium became smooth except for the two scars caused by the ulcers, the opacity remained concentric and thickened at the center. Vision had increased by the following November to 20/40 through the dilated pupil. The patient was seen one year later and the picture remained the same.

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SACCULAR HERNIATION OF VITREOUS INTO ANTERIOR CHAMBER*

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According to Duke-Elder[1] herniation of the vitreous falls into three types: (1) Following intracapsular extraction, (2) following discission of lens or after cataract extraction, (3) following dislocation or subluxation of the lens.

Paulo-Santos[2] believes that vitreous herniation following intracapsular extraction is formed from that part of the vitreous corresponding to Cloquet's canal.

The present paper deals only with vitreous herniation following dislocation or subluxation of the lens. Since the literature reports so few cases of this nature, it must be a rare condition; no similar cases have been found in the English language. In 1946, Poirier[3] reported a case of vitreous prolapse following laceration of the lens with subsequent lens absorption. In our case the lens was intact.

In 1919, Hesse[4] reported nine cases, eight of traumatic origin and one spontaneous. These nine cases were all similar to the present report although differing in details. One was almost identical with ours even to the point at which one observer thought that the vitreous herniation was the edge of a luxated lens until slitlamp examination proved otherwise.

Hesse's case varied in that there was spontaneous recession of the saccule; it was nontraumatic in origin and occurred in a 14-year-old boy with malignant myopia and a detached retina. His other cases varied in the position of the herniation and in the number of saccules, one case having three vitreous protrusions into the anterior chamber.

Two cases[6] one by Haab, 1900, and the other by Seigfried, 1896, were parallel in type to the case herein reported. Paulo-Santos,[2] reported the case of a 50-year-old Japanese who was struck in the right eye by a piece of wood and, 42 days later, had a vitreous herniation into the anterior chamber between the 7- and 11-o'clock positions. In his opinion this case proved the existence of a limiting membrane of the vitreous.

CASE REPORT

History. G. W., a 56-year-old Negro day laborer, was seen in the eye clinic of John Sealy Hospital on June 3, 1948, with the complaint of "black eye."

He stated that he had been struck in the left eye by a man's fist one-half hour prior to examination. Vision had been cloudy

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since the blow but aside from generalized tenderness in the region of the eye he had had no ocular pain.

Eye examination. Vision was: R.E., 20/20; L.E., 20/100. (Vision was obtained using the illiterate "E" chart.)

Two small lacerations were present over the upper lid of the left eye. Both lids were ecchymotic. The bulbar and palpebral conjunctiva showed scattered hemorrhages. The

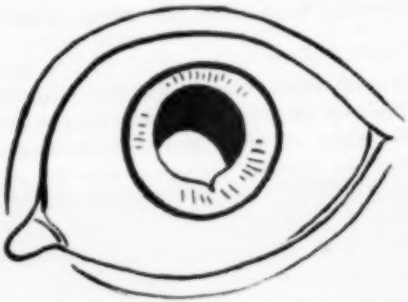

Fig. 1 (Sykes and Dodson). Herniation of vitreous into anterior chamber.

pupil was one third dilated and did not react to light or on accommodation. Extraocular muscle function was normal. Intraocular pressure was: R.E., 16.5 mm. Hg. (Schiøtz); L.E., 14.5 mm. Hg.

There seemed, on gross examination, to be a small hemorrhage on the face of the lens in the lower nasal aspect of the pupil. The ophthalmoscope demonstrated that this spot had some slight motion when the eye moved. In the opinion of one examiner this hazy area represented the upper part of the dislocated lens. A small area of discoloration was seen in the nasal vitreous and this was attributed to the presence of blood. No retinopathy was present.

Slitlamp examination of the left eye revealed that the supposed blood deposit of the anterior capsule of the lens was an accumulation of pigment granules in a small saccular prolapse of the vitreous into the lower nasal aspect of the anterior chamber. There was no difference in depth of the anterior chamber over the area of prolapse as compared to the opposite side. Iridonesis was present but the lens seemed to be in good position and nontremulous.

This prolapse of vitreous measured about three mm. in diameter and at no spot touched the cornea. The cornea was clear and no other pathologic condition was seen (fig. 1).

The right eye was normal.

Treatment. A one-percent atropine ointment was used in the eye and the patient was again seen four days later. The vitreous prolapse was enlarged at this time, measuring about seven mm. horizontally by three mm. vertically. Much of the pigment in and on the surface of the prolapse had disappeared. Vision of the left eye at this visit was 20/70 with the illiterate "E" chart.

This patient has been seen periodically over the past six months during which time the prolapse has gradually enlarged and the membrane covering the prolapse has become thinner in appearance. Figure 1 was made on the first visit. Pictures were repeated on three other occasions but at no time was the vitreous prolapse visible probably due to the scarcity of pigment.

Cowan[6] describes a definite limiting membrane covering the face of the vitreous. He reports this as a nonnuclear, structureless, uniformly staining membrane. He states that, in cases of vitreous prolapse into the anterior chamber, this membrane is fairly easily seen with the slitlamp. A clear zone is usually seen between the membrane and the vitreous body.

This clear zone between the membrane and the vitreous body was present in our case and this would seem to corroborate Cowan's contention. Cowan further stated that this membrane might be a proliferation of the vitreous surface but is never a condensation of that surface. Other investigators believed the hyaloid membrane to be a condensation product of the vitreous similar to the membrane formed on milk or soap solutions.

SUMMARY

A rare case of vitreous herniation into the anterior chamber following minimal subluxation of the lens is presented. A short review of the very scant literature on this subject is included.

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MODIFICATION OF LUEDDE EXOPHTHALMOMETER

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The exophthalmometer of Luedde, although its inadequacies as a measuring device are well recognized, is a useful little instrument that will not readily be displaced for all purposes by more elaborate and expensive exophthalmometers.

Its chief defects are: inconstancy of positioning on a more or less broad segment of the lateral orbital margin; inconstancy in the direction of the instrument with respect to the sagittal and transverse planes of the head; inconstancy in the position of the sighting eye and in the direction of gaze of the patient's eyes. None of these factors can be precisely duplicated at reexaminations.

The Luedde exophthalmometer, as it is now arranged, is calibrated in centimeters subdivided by millimeter vertical markings. On one face, centimeter lines are marked by numbers 1, 2, 3, and 4 denoting the distance from the lateral orbital margin. Each number is duplicated by a similar number below it which is upside down. The opposite face is marked by heavier grooves representing the centimeter distances.

In use, one sights through the marked faces of the instrument to the observed eye. The numbered centimeter lines are kept in the same plane as the grooves on the opposite face. If this is done properly, one is then sure that the instrument is being held in a line perpendicular to the one joining the sighting eye to the corneal apex of the examined eye.

There is such a profusion of vertical lines on the two marked faces that sometimes one has difficulty in precisely sighting the cornea of the patient's eye through them.

The suggestion has been made that one of the sets of centimeter numbers be removed and placed in a corresponding position on the opposite face bearing the centimeter grooves, with both sets of numbers right side up. A Luedde exophthalmometer with this modification makes it possible to line the corresponding numbers readily one above the other.

This small change does not make the Luedde exophthalmometer an instrument of precision, but it minimizes one of its defects.

1777 Grand Concourse.

ERRORS IN ILLUSTRATIONS AND DEFINITIONS OF ACTIONS OF EXTRAOCULAR MUSCLES

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It must be apparent to any ophthalmologist who does a fair amount of squint surgery that there is a discrepancy between the textbook illustrations and definitions of the

extraocular muscles and the actual facts. This is very confusing and misleading.

Terminology

First of all, there must be a common understanding on terminology. The phrases "up and in," "down and in," "up and out," and "down and out" are accepted in descriptive anatomy to define the course taken by blood vessels, nerves, muscle fibers, and movements around joints like the shoulder and hip. The "in" refers to the midplane of the body; the "out" refers to motion or direction away from the midplane.

Fig. 1 (Ambrose). "The muscle triangle."

In the case of the eyes, "in" refers to a nasal direction and "out" refers to a temporal direction. "Up" of course is cephalad and "down" is caudad.

Another common understanding should be the position of illustration and recording. This, in my opinion should be done as viewed by the examiner so that the patient's right side is the examiner's left side, and should not be recorded as if the examiner or reader is behind the patient and looking through a theoretically transparent head. The patient has no idea of what position his eyes are in unless he looks in a mirror.

The next common starting point should be that the examiner learn to think of nine squares around the patient's head—which is the middle square—and to conceive the various positions of gaze as taken from this as a center. The patient's head must be held immobile; if it is allowed to move, the measurements are useless. This study of deviations in the nine squares is a prerequisite to correct diagnosis for it takes the various muscles into their respective fields of action, determines the fixing eye in each field, shows up paretic muscles, and overactions of the yolk muscle and direct antagonist depending upon the fixing eye. This latter study determines the surgical attack which centers around an "eternal triangle," at one end of which is the paretic muscle, at the other end of the hypotenuse is the contralateral yolk muscle, and at the end of the short arm is the direct antagonist (fig. 1).

Consideration of binocular movements

Another common ground should be the consideration of binocular movements of the eyes. This gives more information than monocular study, although the latter should not be omitted.

Taking a muscle into its field of action tests the integrity of its nerve supply the same as testing any other skeletal muscle and its nerve supply. As far as muscle surgery is concerned, this main action of a muscle in its field is the only one to be considered, the subsidiary actions can be ignored; of these two, the more important is intorsion by the muscles attached to the upper part of the globe namely the superior oblique and the superior rectus; and extorsion by the muscles attached to the lower part of the globe, namely the inferior oblique and the inferior rectus.

Least important is ADDuction attributed to the vertical recti and ABduction attributed to the obliques. In order for the former function to take place, the globe must be brought nasal to the midplane of the orbit. This presupposes an intact medial rectus, paresis of which cannot produce adduction even in the presence of normally acting vertical recti. A paretic medial rectus also prevents full oblique muscle action due to the same failure of the globe to be brought into the nasal field. In order for ABduction, by the obliques, to take place, one must presume a normally acting external rectus to bring the globe temporal to the midplane of the orbit. With a weak externus, the obliques cannot ABduct, and neither can full vertical rectus action take place under the same circumstance. One can convince himself of these facts by careful

study of movements in the case of an isolated paralysis of either the lateral or medial rectus.

Assume that in the middle of this page there is pictured the RIGHT eye. The upper left-hand corner would correspond to a direction called "up and out" denoting one continuous motion—it could also be termed "up and temporally" or as a right-hand elevator in the temporal field—this is the function of the right superior rectus. By no stretch of the imagination can one say that the right superior rectus takes the eye "up and in" as is described and pictured in various textbooks.

The upper right-hand corner of the page corresponds to a direction called "up and in" denoting one continuous motion—it could also be termed "up and nasally" or a left-hand elevator in the nasal field—this is the field of action of the right inferior oblique—it turns the eye "up and in." By no stretch of the imagination can it be said to turn the eye "up and out."

The lower left-hand corner of the page would correspond to a direction "down and out" or "down and temporally," or a right-hand depressor in the temporal field—this is the field of action of the right inferior rectus muscle—it turns the eye "down and out." By no stretch of the imagination can it be said to turn the eye "down and in."

The lower right-hand corner of the page corresponds to a direction "down and in" or "down and nasally" or to a left-hand depressor in the nasal field. This is the field of action of the right superior oblique. By no stretch of the imagination can it be said to move the eye "down and out."

These erroneous definitions of action of the muscles make as much sense as saying the 20th Century Limited runs east and west—it may but not the one train at the same time. The correct representation of the directions for the muscles of the right eye are shown in Figure 2.

Now imagine that the left eye is pictured in the center of this page. The upper right-hand corner would be "up and out" or "up and temporally," or a left-hand elevator in the upper temporal field. This is the field for the left superior rectus. It turns the eye "up and out" and not "up and in."

The upper left-hand corner of the page is the direction "up and in" for now the left-hand edge of the page corresponds to a nasal position; it could also be called "up and nasally" or a right-hand elevator in

Fig. 2 (Ambrose). Correct representation of the directions for the muscles of the right eye.

the upper temporal field. This is the field for the left inferior oblique. It turns the left eye "up and in," and not "up and out"—it just can't do that.

The lower right-hand corner of the page corresponds to a direction "down and out" or "down and temporally," or a left-hand depressor in the lower temporal field. This is the field for the left inferior rectus—it turns the eye "down and out" but not "down and in."

The lower left-hand corner of the page would represent a direction "down and in" —or depression in the lower nasal field or a right-hand depressor in the lower temporal field. This is the field for the left superior oblique—it turns the eye "down and in" and not "down and out." The directions for the left eye muscles would then be as shown in Figure 3.

Now, to consider both eyes binocularly—when the right superior rectus is in its field of action—"up and out," its yolk muscle, the left inferior oblique, is in the "up and in" position. There is positively no reason to

say that this muscle is taking the eye "up and out" just because its contralateral yolk muscle, the right superior rectus, has the eye in the "up and out" position. Both these muscles acting together are "right-hand elevators in the upper temporal field" though the position of the left inferior oblique is "up and in" regardless.

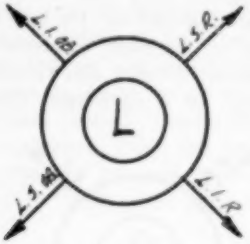
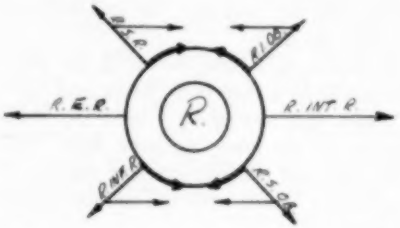


Fig. 3 (Ambrose). Correct representation of the directions for the muscles of the left eye.

The depressors in the right lower temporal field are the right inferior rectus and its yolk muscle the left superior oblique, the former bringing the eye "down and out" while the latter simultaneously brings the left eye "down and in."

The elevators in the left upper temporal field are the left superior rectus for the left eye and right inferior oblique for the right eye. The depressors for the left lower temporal field are the left inferior rectus for the left eye and the right superior oblique for the right eye.

An understanding of these points is helpful not only in the diagnosis and treatment of squints, but it also serves for a clearer understanding of the diplopia field study, especially after secondary contractures of the yolk and direct antagonist muscles have taken place.



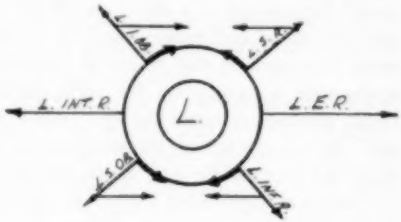


Fig. 4 (Ambrose). Correct representation of the main action of the vertical muscles, as well as their subsidiary actions of torsion, adduction, and abduction.

Errors in textbooks

Space does not permit more than passing mention of the errors in illustrations and definitions of the extraocular muscle actions found in many of the standard ophthalmic textbooks. The examples given here can be multiplied many times.

War Department Technical Manual (8-300) November, 1940.

Figure 13, page 118—The arrows labeling the action of the vertical muscles of the right eye are in reverse of the correct direction.

Figure 14, page 119—The arrows labeling the action of the conjugate or yolk muscles of the two eyes (shown together) are in reverse.

Page 120—The table labeled "Conjugate Muscles" gives credit to the right inferior oblique and the left superior rectus for eyes "up and to the right." This should be for eyes "up and to the left." The muscles named for the other oblique positions are also incorrect.

The Anatomy of the Eye and Orbit. By Eugene Wolff. Philadelphia, Blakiston, 1933.

Figure 74, page 135—Both eyes face the examiner. The "superior rectus" legend should be on the arrow for the inferior oblique for each eye. The "inferior rectus" should be on the arrow labeled "superior oblique." With these corrections, the curved arrows denoting torsion would have to be changed.

Line 4, page 135—"The superior rectus makes the eye look upward and inward"—should read "up and out."

Line 16, page 136—"The inferior rectus makes the eye look down and in"—should read "down and out."

Line 27, page 139—"The inferior oblique makes the eye look up and out"—should be "up and in."

Practical Neurological Diagnosis. By R. Glen Spurling. Springfield, Illinois, C. C Thomas, 1935. Figure 11, page 32—In this illustration of both eyes and their external muscle action, the labels at the ends of the directional arrows are opposite to fact.

Conclusion

Figure 4 will, I believe, clarify the erroneous impressions created by the misstatements herein listed. This chart shows the main action of the vertical muscles in their "fields," as well as their subsidiary actions of torsion, adduction, or abduction.

15 Washington Street (2).

I am grateful to Dr. Lee W. Hughes for encouragement to write this paper, to Dr. Rudolf Aebli, and to the late Dr. James W. White who read the original draft of this paper and with whom I discussed the material on several occasions.

ARGYROLENTIS

Emanuel Rosen, M.D.
Newark, New Jersey

Only an occasional reference has been made to the occurrence of silver within the human lens. Duke-Elder[1] says that "in endogenous cases pigmentary deposits (of silver) occur, although more rarely in the inner eye. This is more particularly seen in the lens capsule." Duke-Elder refers to an article by Alt.[2] However, a careful study of Alt's case failed to uncover any reference to the presence of silver within the lens.

Alt's patient, after three months' treatment with silver nitrate and argyrol, developed argyrosis of the conjunctival tissue. A biopsy of the conjunctival tissue was done, but there is no reference to lens involvement.

In 1930, Friedman and de Roetth[3] pointed out that the occurrence of argyrosis of the conjunctiva was so common that the presence of argyrosis of the cornea was frequently overlooked. In two of the 12 patients they examined, there was only slight silver staining of the conjunctiva. In the other 10 patients, however, they observed a distinct golden to greenish-blue coloration of the posterior corneal surface. In some of the cases, there was a similar golden reflex from the anterior capsule. In others, the posterior capsule and the subcapsular part of the posterior cortex were yellowish in color.

In Case 1 reported by Friedman and de Roetth, in addition to the usual biomicroscopic findings in argyrosis of the conjunctiva and cornea, it was noted that the anterior capsule of each lens produced a very marked golden reflex, more intense in the lower periphery and gradually becoming less intense toward the center. The posterior capsule and the adjacent layers of the posterior cortex imparted a golden glow, most apparent by retro-illumination. No opacities were present. The patient had been using two drops of silver nitrate almost daily for seven years.

Recently, Loewenstein[4] reported a woman, aged 72 years, with cataract, incipient in one and more advanced in the other eye. She was given argyrol ointment to be used for four days prior to operation. When she returned a year later, she had a marked argyrosis, and it was learned that she had used the ointment daily for the whole period. After the cataract was removed, examination failed to reveal any silver in the lens capsule.

In histologic studies of excised argyrotic conjunctiva and tear-sac, Loewenstein was able to demonstrate that the epithelium did not store any silver particles either within the conjunctiva or in the tear-sac.

The silver particles were situated predominantly in fibers and ribbons corresponding to the elastic system. Beside the silver particles stored within the elastic fibers, he found free particles in the tissue, sometimes in larger clusters, and within the endothelial cells. The greatest portion of the silver particles, however, were bound to the elastic fibers; a much smaller number being situ-

ated free within the connective tissue; other silver particles were "phagocytised" by the reticulo-endothelial cells of precapillaries and capillaries.

Loewenstein concluded that the silver was precipitated as AgCl, and possibly reduced under the influence of light to metallic silver. The "elastophilia" of silver as observed in his case offered new prospects in experimental work.

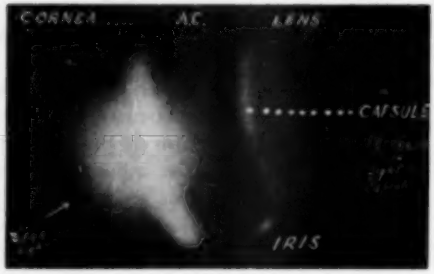


Fig. 1 (Rosen). Slitbeam photograph of eye showing argyrolentis.

Case report

History. Dr. M. W., a 42-year-old dentist, was referred for refraction, his complaint being headaches and fatigue, but no visual disturbance. He had never worn glasses and had never had any ocular disturbance. His wife had recently suffered a coronary occlusion, which apparently had had some influence upon the production of his cephalgia, asthenia, and general lassitude.

In recording the history it was learned that in his work he had been "pushing amalgams" for many years. This he had always done upon the palm of his hand. His patients came from a rather poor economic level, a fact which he considered important, since it indicated that most of his work was limited to this type of dentistry.

Eye examination showed a visual acuity of better than 20/20 in each eye. There was no involvement of his lids, pupillary reactions, or muscle balance. The conjunctivas were quite clear.

There was a slate-blue-gray ring, just anterior to the endothelium, in the cornea, which started close to the limbus and extended for two mm. centripetally. There was a slight yellowish tinge toward the periphery. This symmetrical ring was bilateral.

Fig. 2 (Rosen). Argyrolentis.

Just within the anterior capsule of the lens, there was a small metallic disc, 3 by 3.5 mm. in diameter (figs. 1 and 2) which was made up of very minute deposits of

small grayish-blue circles. From the periphery of the disc several faint rays spread out. The appearance was not unlike that of a "sunflower" cataract which is seen when copper is present in the eye. Otherwise the lens was crystal clear even in the posterior capsule.

This lens change was restricted to the pupillary area and did not extend beyond the pupillary margin. The vitreous showed no abnormality. The fundus was normal except for the presence of medullated nerve fibers (fig. 3).

Physical examination showed no further abnormalities. Spectrographic analyses of urine, feces, and blood indicated the presence of the following elements, in diminishing amount: Mercury, zinc, tin, copper, lead, and silver. Chemical analysis of the urine gave 33 mg. mercury per 100 cc. The possibility of Wilson's disease with its attendant "sunflower" in the lens was considered but neurologic examination was completely negative.

Discussion

It is known that in the 17th century, when it was fashionable to treat epilepsy, tabes, and all manner of incurable diseases with vast quantities of silver internally, it was not at all uncommon for patients to be turned permanently dusky or even black. No biomicroscopic studies were made at that time and so argyrolentis may have been present but unrecognized.

It was not until 1927 that the first slitlamp picture of this condition was published by Larsen[5] who described several cases among silversmiths in whose lenses deposits of silver were found. He considered the formation of a subcapsular lens disc an original observation, no previous case having been reported. Yet he refers to four cases reported by Schnaudigel in 1913.[6]

Duke-Elder has stated that the action of silver is not unique, since all the heavy metals, such as lead, copper, gold, and platinum, as well as silver, tend to produce granular deposits.

Argyrosis may be either local or general. In the first instance a silver preparation is applied locally, and the pigmentation is confined to the part of the body concerned. In the second instance, silver is given internally in the course of therapeutics or is absorbed in quantity industrially, in which case every organ of the body may become affected.

Fig. 3 (Rosen). Fundus photograph, showing medullated nerve fibers.

Loewenstein has stated that argyrosis of the conjunctiva arises not only after local use of silver, but also when this is administered orally and intravenously. Duke-Elder states that it is a rare exception for a general argyrosis to follow a local one; that this occurs only when the local facilities of absorption are singularly intensified, as in the treatment of extensive burns with silver (Olshausen,[7] 1893; Crusius,[8] 1895).

In local argyrosis the conjunctiva is usually most markedly affected; in general argyrosis, the cornea is the most susceptible tissue.

It has been shown that argyrosis may be produced experimentally, for Zur Nedden,[9] in 1906, produced opacities of the cornea experimentally with the heavy metals, and found that silver was precipitated as silver

mucoid, and possibly as a silver albuminate, carbonate, and chloride. He could also distinguish a black silver precipitate in all these chemical combinations.

Conclusion

The finding of a disclike metallic "sunflower" during the course of an ocular examination may indicate absorption of a metallic element through usage over a period of years. The lens should be studied carefully, and any abnormality appearing therein should be given careful consideration.

692 High Street (2).

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8. Crusius: Cited by Duke-Elder.[1]
9. Zur Nedden: Cited by Duke-Elder.[1]

OINTMENT IN THE ANTERIOR CHAMBER

Peter Sykowski, M.D.
Schenectady, New York

Recently, Meek[1] stated that it was a "mistake to fill the conjunctival sac with ointment after any intraocular operation because of the danger of the ointment being drawn or forced into the anterior chamber."

Binder[2] reported a case of ointment in the anterior chamber following a penetrating corneal wound for the removal of which surgery was performed.

Smith[3] wrote of "several instances of ointment globules after operation for cataract prior to the introduction of closure of the section with corneoscleral sutures;" furthermore, he reported that "it was not necessary to open the anterior chamber to remove the globule because the antiseptic salve always absorbed."

Observation of two cases in which ointment globules were present in the anterior chamber following cataract surgery are herewith reported.

Report of cases

Case 1. A. L., a 60-year-old white man, had a combined intracapsular cataract extraction in September, 1947. Through an error, atropine ointment was instilled into the cul-de-sac. Because the patient was a "squeezer," it was impossible to examine the operated eye until the third postoperative day.

On this day a round, solid, grayish globule approximately three mm. in diameter was observed in the anterior chamber in the center of the pupillary area. On the 10th day the globule was still present, but smaller. On the 14th day biomicroscopy revealed a solid globule about one mm. in size in the 12-o'clock area of the anterior chamber. On the 21st postoperative day there was no evidence of the foreign matter.

Case 2. M. N., an uncooperative 80-year-old woman, had a combined intracapsular cataract extraction in November, 1947. Similarly, through error, atropine ointment was instilled into the cul-de-sac postoperatively.

On the third postoperative day, two globules were present—an air and a solid globule, the former being larger. On the seventh day the air globule was absorbed, and on the 16th day there was no evidence of the solid foreign body.

Comment

In both cases, intracapsular cataract extractions were performed, thereby eliminating the likelihood of cortical or of capsular material as etiologic agents. It was not necessary in these cases to intervene surgically for the removal of the ointment globules. Fortunately, neither immediately postoperatively nor during the convalescent period was there any dangerous sequela.

1330 Union Street (8).

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KERATOCONUS POSTICUS GENERALIS

Joseph V. M. Ross, M.D.
Berwick, Pennsylvania

Abnormalities of the curvature of the cornea are not too common. A general classification of the supposedly developmental, nonacquired types is: (A) Those involving the entire cornea and therefore both corneal surfaces—1. cornea plana, and 2. keratoconus, or conical cornea; (B) More rarely, those in which only the posterior corneal surface is involved (Butler believes this to be more common than keratoconus but overlooked)—1. keratoconus posticus circumscriptus, a localized variety, and 2. keratoconus posticus generalis, a uniform variety.

In the keratoconus posticus types the anterior curvature is smooth, regular, and of average radius and the cornea is thinned in the area of increased curvature. In the circumscriptus type, there is a small, localized area of increased posterior corneal curvature and it is believed due to trauma and/or local corneal disease and/or heredoconstitutional factors.

In the generalis type there is an unusually short radius of curvature for the entire posterior corneal surface which is said to be perfectly regular, but this would be hard to prove. This type is believed to be only heredoconstitutional or developmental. It is apparently not progressive, usually is not bilateral, occurs at birth, and, although the corneal stroma is thinned, there is not great impairment of vision since the alteration in curvature at the face is in contact with aqueous fluid.

The following is a report of a case of this unusual but interesting abnormality with bilateral involvement.

Report of a case

M. B., a white woman, a widow, aged 62 years, whose present general health was good and whose family history and past history were essentially negative, stated that she had worn one pair of glasses only for the past six years and these only for close work since her far vision had always been fairly good. Of late, following intranasal penicillin therapy for a cold, she stated her eyes have begun to annoy her for near, and close questioning seemed to reveal that, apparently, she had just become more conscious recently of presbyopic phenomena. There were no other complaints.

External examination of the eyes was essentially normal except for a slight bilateral meibomitis with angular whips. Muscle balance was normal; there were three degrees of fusion.

Vision unaided was: O.D., 20/40; O.S., 20/50; 0 at 14 inches, O.U. Vision with correction of: O.D., +1.25D. sph. =

20/40; O.S., +0.75D. sph. = 20/50; with +2.0D. sph., O.U., 6 pt. type at 14 inches.

Her old (and only) prescription was +2.75D. sph., O.U., which she used for near only. Tension, O.U., was 15 mm. Hg (Schiøtz). Fields were normal. All the usual laboratory studies were normal.

During retinoscopy it was observed that there was an intense scissors movement, with a dark intervening band and a fainter peripheral with movement in each eye. It was interesting in that unaided vision could not be improved for far with lenses but that the same vision could be obtained with: O.D., +1.25D. sph. = 20/40; O.S. +0.75 D. sph. = 20/50. Or: O.D., +3.25D. sph. ⌒ −4.0D. cyl. ax. 108° = 20/40; O.S., +2.75D. sph. ⌒ −4.0D. cyl. ax. 72° = 20/50. However the patient was, by trial-frame test, much more comfortable with the former prescription which was, therefore, given. (The law of spherical equivalents was here apparent.) The patient is comfortable now with glasses. Contact lenses did not improve vision.

Ophthalmoscopic findings were essentially the same in each eye. There was a peculiar central corneal glint and a horizontal dark band below the glint was surrounded by a normal fundus reflex. The fundi were hazy. There were a few large vitreous opacities in each eye. The discs revealed coni nasally and temporally and elsewhere presented indistinct margins, but no edema. There were a few colloidal masses scattered throughout both fundi. There was a generalized choroidal sclerosis and retinal angiosclerosis, Grade 2, O.U. The fundi were tessellated and with indistinct macular areas.

Biomicroscopy likewise was essentially the same in each eye. There was a slight bilateral arcus senilis. In the lower half of the cornea in each eye was a Fleischer or Stähli-Hudson line, wavy, tenuous, horizontal, thin, yellow-brown to brownish green in color. The pigment was in the corneal epithelium and possibly Bowman's membrane but the stroma was not invaded. The line extended within three mm. of each limbus in each eye. The corneal stroma was thinned but uninvolved otherwise. There was an endothelial reflex. The anterior corneal curvature was normal but the posterior was definitely increased smoothly and uniformly. In each eye near the periphery scattered here and there were a very few Hassal-Henle bodies. There was no evidence of other anterior segment disease.

Discussion

This patient apparently had had this corneal abnormality all her life. Of course, of this one can not be certain. In checking with the optometrist who had given her her other pair of glasses six years previously, her vision was the same as at this writing, so the condition is nonprogressive to date.

One of the thoughts that occurred to me was whether this was an arrested, early stage of true keratoconus. In the posticus variety the cornea withstands the normal intraocular pressure and maintains its normal anterior curvature in spite of stromal thinness. Duke-Elder states that the shape of the cornea in this condition approximates the embryonic state, and the anomaly is probably an arrest of development resulting in the persistence of an embryonic character. It might be that in true keratoconus some abnormalities of the entire cornea are superimposed on the arrested development.

At any rate in the case herein presented there certainly are many findings not characteristic of the keratoconus we recognize as a clinical entity today. Among these differences are: (1) Contact lens does not help; (2) the condition is apparently not progressive; (3) there is no "dewdrop" luster; (4) the retinoscopic picture is different; (5) the ophthalmoscopic picture (at a distance) is different; (6) although a Fleischer line was present, it was really a line, and not a ring, so it probably is better named a Stähli-Hudson line; (7) the other

slitlamp findings were distinctly different from those of the usual keratoconus and concluded a diagnosis of keratoconus posticus generalis.

The diagrammatic illustration (fig. 1) of the types of abnormal curvatures of the cornea believed due to heredoconstitutional and heredodegenerative factors helps one to visualize these abnormalities. Trauma and inflammation are suspected causes; if they are the true causes, however, the present classification is in error, and similar types of abnormal curvature of the cornea due to these same and related causes (acquired) must be included in a broader classification.

321 East Front Street.

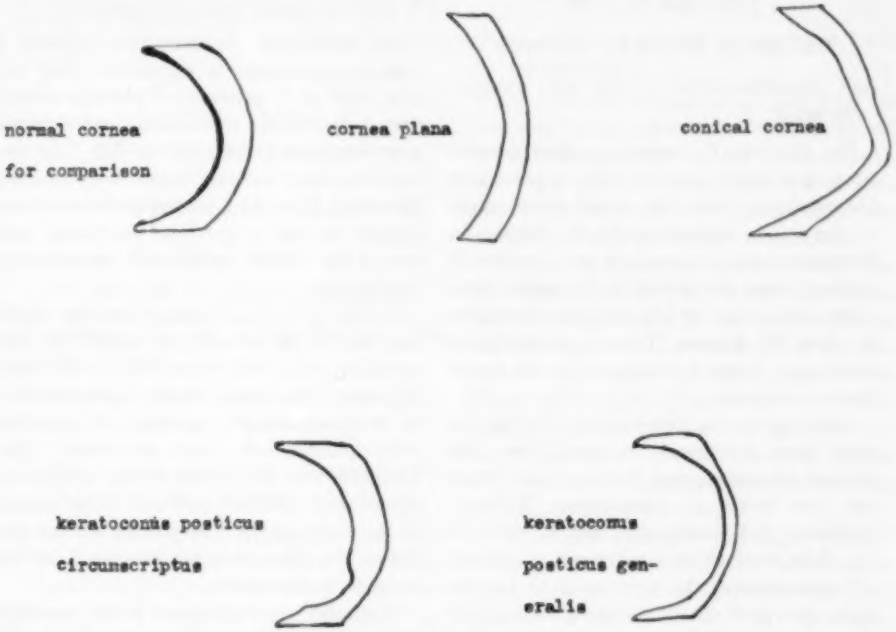

Fig. 1 (Ross). Diagrammatic illustration of the types of abnormal curvatures of the cornea allegedly due to heredoconstitutional and heredodegenerative factors. A normal cornea is shown for comparison.

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SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

September 29, 1949

DR. DEANE HARTMAN, *chairman*

AN INTERPRETATIVE STUDY OF HETEROPHORIAS

DR. SAMUEL V. ABRAHAM, after demonstrating research on this subject, presented his conclusions that the actual visual angle of the eye is approximately 45 degrees in divergence, as the eye has not completely evolved from the primitive divergent state. After some years of life, the angle decreases to about 20 degrees. There is probably no divergence center as compared to the center for convergence.

Convergence is developed to bring the eyes from divergence to parallelism, and further to convergence for near use. There are two levels of convergence function, voluntary and involuntary, and the latter is the older level. With a minimum of activity of convergence, the eyes tend to become more divergent, that is assuming their primitive positions. This occurs especially when anything interferes with binocular vision as in occlusion.

There is a definite relationship of convergence function to muscle balance and a relation of convergence function to fusion faculty. Convergence is the strongest function. The convergence spasm may be completely relaxed with cycloplegics. Vertical phorias may be overflow of stimuli to vertical muscles in a similar manner to medial rectus spasm causing esophoria. Phorias are not precursors of strabismus but represent the convergence effect on the position of rest.

The principles and rules for therapy were presented. Dr. Abraham emphasized cooperation and the coördination of orthoptics, surgery, and office procedures.

A CASE OF SCLEROMALACIA PERFORANS

DR. PHILIP D. SHANEDLING, reported a case of scleromalacia perforans. The patient had as a generalized physical condition, polyarthritis deformans, and multiple granulomatous lesions of the skin. The eye had been blind for three years with absolute glaucoma. Five small craterlike defects were present in the subconjunctival tissue, and one at the limbus perforated, necessitating enucleation.

In the pathologic presentation the sclera was seen to be necrotic and walled off with epithelial cells, with sequestration and disintegration. The abscess showed a central mass of necrosis which consisted of epithelial cells, plasma cells, and fibroblasts. This condition may be similar to the nodules of rheumatoid arthritis and are quite similar in the early stages. The lesions seldom perforate the sclera, but may perforate at the corneoscleral junction.

According to the reports in the literature these patients are usually under 50 years of age and may have rheumatism and arthritis, but the association with polyarthritis deformans has not yet definitely been established.

CANCER OF THE BREAST WITH METASTASIS TO THE ORBIT

DR. JACK FIELDS reported that cases of metastasis to the orbit are infrequent. This condition occurred six years after mastectomy for carcinoma. The patient had a vision of 20/20 with a palpable mass in the orbit, and an exenteration was performed. X-ray and radium therapy and testosterone injections were given. Nine months later the seriologic test for cancer was negative. The

pathologic studies showed invasion of scleral tissue in the eye, which still had normal vision.

The methods of diagnosis and treatment were reviewed and the rarity of the condition emphasized. The discussant showed the paths of spread of carcinomatous tissue. In this type of case there is usually permeation along the lymph vessels, here probably latent to one of the bones of the orbit.

Orwyn H. Ellis,
Recorder.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

May 2, 1949

DR. BENJAMIN ESTERMAN, *president*

MEASUREMENTS OF ACCOMMODATION AND CONVERGENCE

DR. JOSEPH PASCAL discussed this subject during the instruction period.

EFFECT OF PROCAINE UPON THE SPHINCTER MECHANISM OF THE PUPIL

DR. HAROLD G. SCHEIE said that previous work had shown that retrobulbar injections of procaine produced the effect of a temporary ciliary ganglionectomy. The pupil on the injected side was dilated and fixed, as Anderson had found in 1903 while working with cats from which he had removed the ciliary ganglion. Physostigmine no longer produced miosis but pilocarpine remained effective. The effect persisted for 80 to 90 minutes in dogs and 1 to 5 hours in man.

Procaine applied locally to the iris by injection into the anterior chamber produces a marked mydriasis which is resistant to all miotic agents. If dropped into the conjunctival cul-de-sac in solution with a detergent, absorption into the anterior chamber is also sufficient to cause mydriasis. Twenty of 27 human subjects showed mydriasis following two instillations of 10-percent procaine with 1:3,000 phemerol. A mild cycloplegic action was also observed occasionally. Procaine was thought to have a direct depressant action on the cells of the sphincter muscle of the iris because pupils dilated by anterior-chamber injection failed to constrict to any type of miotic agent including those which stimulate the muscle cell directly, such as calcium ions.

SOME EXPERIENCES IN SUBTROPICAL OPHTHALMOLOGY

DR. ARYAH FEIGENBAUM said that the seasonal acute ophthalmias caused by the Koch-Weeks bacillus and the gonococcus respectively are correlated with the climatic conditions; they show a typical course and parallelism with the mean temperature.

Transition from the endemic to the epidemic period of the Koch-Weeks ophthalmia finds its explanation in the hibernation of the bacillus in an inactive state on the conjunctiva of some individuals; this is followed by a rapid spread of the extremely infectious disease as soon as the agent becomes activated through lowering of the resistance in the conjunctival tissue during the long and dry summer.

Gonococcal epidemics, the main cause of blindness in the Middle East, seem to become most deleterious in years with great number of sirocco days. There is a close interrelation in backward countries between the epidemic conjunctivitis and the spread of the low-infective trachoma. Trachoma does not play today an appreciable role in Israel.

Since 1939, exhaustive studies have been done on epidemic keratoconjunctivitis. Manifestation of vernal catarrh is often due to the factor of dryness and light on susceptible persons. Cutaneous leishmaniasis affecting the superficial layers is localized in the palpebral skin in about 2.5 percent of the cases, and ectropion of the lower lid is caused by superimposed infection. Relapsing fever was studied experimentally and the late manifestations were most probably due to toxic

action. While during the attacks the aqueous humor of apparently healthy eyes of experimental animals always contains spirochetes and is infective, the spirochetes cannot be demonstrated when the eye itself is infected, the aqueous of which is noninfective.

The occurrence of ocular leptospirosis (uveitis) caused by a local bovine strain of leptospira was reported for the first time in the literature in 1948. In leprosy, interstitial keratitis has been observed as being always secondary to a primary infection of the episclera or ciliary body.

Behcet's disease, observed only in persons of oriental extraction, is characterized as a manifestation of a chronic septic condition (main agent Staphylococcus aureus) connected with a constitutional disorder (mainly latent tuberculosis).

Sirocco days, which interfere with the water balance of the body and the sodium and chloride contents of the tissues, show a definite influence on the tension of glaucoma patients in whom usually an increase of intraocular pressure can be observed a day or two after the sirocco weather has passed.

INSTRUMENT FOR EARLY DETECTION OF MACULAR ABNORMALITIES

DR. MAX GOLDSCHMIDT said that edema of the macula, due to various causes is very difficult to detect in the beginning stages. These difficulties can be overcome by applying the phenomenon of Haidinger's brushes.

The slightest anatomic or physical change of this part of the retina makes the polarization effect disappear. Therefore, the phenomenon of Haidinger's brushes can be applied for clinical use.

An instrument was so constructed that, with the use of filters, the phenomenon could be made visible in everyone, independent of age, aphakia, and, to an extent, degree of vision.

The instrument permits one to decide whether an anatomic macula is absent, as in albinism, nystagmus, and special cases of strabismus. In strabismus, it is possible to decide whether exercises or treatment for improvement of amblyopia are advisable or not. There is also the possibility of making a differential diagnosis between macular disease and retrobulbar neuritis in their earliest stages. It is suggested that this phenomenon, in its application to clinical cases, be called Haidinger's polarization test of the fovea centralis.

Bernard Kronenberg,
Recording Secretary.

COLORADO OPHTHALMOLOGICAL SOCIETY

December 18, 1948

DR. RALPH DANIELSON, *presiding*

CLINICAL CASES

GUNSHOT WOUND

DR. KAFKA AND DR. EGAN presented a man who had been hunting two weeks ago and was hit by a piece of No. 6 shot which entered the eye at the 5-o'clock position at the limbus. Pfeifer localization showed the shot to be behind the eye. The anterior chamber had been filled with blood which absorbed in three days. At present the fundus is obscured by a massive vitreous hemorrhage.

Discussion. Dr. Droegemuller said that, if there is a possibility of obtaining an eye with useful vision, the injured eye might be retained. There is no use in retaining a totally blind eye. After sympathetic ophthalmia begins, it is too late to enucleate.

Dr. Crisp said one must balance the loss of the eye against possible later loss of the good eye. If this were to occur even a little vision would be useful in the injured eye. A shrunken eye has been known to produce sympathetic ophthalmia from the irritation of osseous formation in the eye.

Dr. Sweigert considers the rarity of sym-

pathetic ophthalmia in the army as due to prompt enucleation. Dr. Long thought sympathetic ophthalmia not so rare and more likely to occur if a foreign body is left in the eye.

Angiosclerosis of retina

Major John Grunwell, Jr., (MC) U.S.A., Fitzsimons General Hospital, presented a 45-year-old man who came six months ago for glasses. His only complaint was failing vision. His vision was: O.D., 20/20, J3-14; O.S., 20/30, J9-14. Corrected vision was: O.S., to 20/25, with a −0.25D. sph.

On fundus examination, the retinal vessels of each eye showed a generalized sclerosis with a diminution in the size of the vessels and local variation in the caliber of the veins. There were numerous pinpoint and flame-shaped hemorrhages of various sizes throughout both retinas, particularly involving the macular area of the left eye. Exudates were present and moderate choroidal sclerosis. The blood pressure was 120/80 mm. Hg.

A thorough medical check and a search for foci of infection revealed only a mild allergic rhinitis. His family history was negative. His wife is a tuberculosis patient at Fitzsimons Hospital.

The following tests were performed: C.B.C., urinalysis, sedimentation rate, prothrombin time, complete blood chemistry, blood sugar, glucose tolerance, renal functional tests, Gothlin index test for increased capillary permeability, muscle biopsy to rule out periarteritis nodosa, daily blood-pressure studies, bone-marrow count, and injection of guinea pig with bone marrow for tuberculosis, 1st and 2nd strength Mantoux tests. All were normal.

During the course in the hospital, the patient was given rutin (60 mg., three times daily), vitamin C (50 mg., three times daily), and a high caloric diet. The eyes were atropinized. The left eye was given 4,000 r of X ray in divided doses.

Hemorrhages in the left eye cleared somewhat but a month later became worse in the right eye. Vision varied from 20/20 to 20/80. The patient is still on rutin and vitamin C, with Koagamin intravenously weekly. Hemorrhages in the right eye appear to be clearing. In the left eye, they remain approximately the same as on admission. There is a considerable amount of neovascularization in the areas where hemorrhages were.

Dr. Grunwell's impression was that the case was: (1) Angiosclerosis of the retinal vessels with secondary hemorrhages and exudates; (2) choroidal sclerosis.

Discussion. Dr. Long suggested that it might be a case of Eales's disease. Dr. Fillmer said it was possible to have Eales's disease without vitreous hemorrhage. Dr. Sweigert suggested massive doses of X rays. Dr. Crisp said he believed that bed-rest and mild heliotherapy would be better than massive doses of X rays.

Dr. Danielson said he had seen a soldier from Guam three years ago who had had retinal hemorrhages with sudden vitreous hemorrhage which were assumed to be secondary to contusion. Later a sinus in the axilla was proved to be tuberculous. Dr. Hassler suggested blood transfusion.

Enlargement of blindspot

Dr. Strong presented a white man, aged 40 years, with a history of always having had something wrong with the left eye. He complained of occasional headaches and lately noticed that the left vision had become worse. Examination showed vision to be: R.E., 20/300, with correction 20/40; L.E., 20/400, with correction 20/50, tactile tension −1. Someone had suggested that he had glaucoma.

Fields were normal except for slight enlargement of the blindspot, especially in the left eye. The retina surrounding the left optic nerve was depigmented in the nasal superior and temporal portion. Two small pigment spots were seen along the bifurca-

tion of the left nasal artery. There was possible swelling of the left optic nerve. Otherwise the fundi and the skull X-ray studies were normal.

Central chorioretinitis

Dr. Chapman presented a woman, aged 49 years, with central chorioretinitis of the right eye. Following a cold she noticed on October 17th, that right vision blurred and letters were distorted. She had been sick a good deal as a child and had a bronchiectasis. The teeth had been recently examined and were in good condition. Externally the eyes were normal. Vision was: R.E., 20/200, eccentric and distorted; L.E., corrected 20/15. The fundus of each eye was filled with drusen, yellowish, of varying size. The right macula had an area of edema of about one-third prism diopter, with pinpoint red dots around it.

A course of sulfadiazine and penicillin was given, as well as typhoid vaccine intravenously. The edema cleared, glistening white deposits appeared around the lesion and a small hemorrhage remained in the macular area. Nitroscleran for vasodilatation had been tried but the central scotoma and vision remain the same. The blurring of the dominant eye at first was very annoying but has now been suppressed, so that the patient is comfortable using the left eye.

Following the presentation of clinical cases, a paper, "Exophthalmos of endocrine origin," was read by Dr. Robert William Vines, instructor in medicine, University of Colorado Medical School.

Katherine Chapman,
Secretary

Ophthalmic Miniature

A proper cure begins with a purgative, using my Jerusalem pills, compounded by me. The formula of these is spurge, half an ounce, hepatic aloes, five ounces, to be ground with sugar of roses. After purgation, at the third hour, the patient should be placed astraddle a bench, as if on horseback. Now be seated on the same bench face to face with the patient, who will keep one eye closed. So begins the operation in the name of our Saviour Jesus Christ.

With one hand raise the upper lid, and with the other hold a silver needle and direct it toward the outer lacrimal region. Then perforate the eye coats, pushing and turning the instrument around with the fingers until you touch the diseased matter, which the Saraceus and Arak call livizaret (but which we call cataract), with the point of the needle, and dislodge it from its position in front of the pupil. Then push it well below, holding it there until you have said four pater nosters. Then carefully and slowly turn the needle back to its first position in front of the eye.

Benevenutus Grassus, *De Oculis*, 1474.

(Translated by Casey A. Wood. Stanford University Press, 1929.)

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THE AMERICAS UNITE TO SAVE SIGHT

What could be more pleasant than a convention in southern Florida during the last week of March? The warm sunshine, the marvelous salt-water bathing, the boat rides, the green grass, the luxuriant vegetation, the mellow breezes—ah! what a relief from the snow and ice for most of us! But that wasn't all—for here we met old friends and made new friends from north, south, east, and west.

The executive officers of the two organizations, the National Society for the Prevention of Blindness and the Pan-American Association of Ophthalmology, decided more than a year ago to unite their efforts in an attempt to show the world that they have a common objective—to save sight—and that they work harmoniously to accomplish it. The National Society for the Prevention of Blindness has an annual meeting in the late winter, or early spring, in some prominent city. The Pan-American Association holds congresses every four years—the last one was in Havana in January, 1948, and the next will be in Mexico City in January, 1952—so this was an interim meeting for them.

The combined program was one of un-

usual interest. There were reports of encouraging progress from many of the countries of the Western Hemisphere, given by the chairmen or members of committees and other individuals. There were reports on new or improved techniques, new drugs, new diets, new problems and their possible solutions, and so forth. It is impossible to mention each contributor by name in a short editorial; and it is not fair to mention a few as giving outstanding reports, because all of the papers were so manifestly excellent.

Among the presentations which seemed especially to please our Latin-American colleagues, as well as our English-speaking members, were the five symposia: one was given mainly by the Latin Americans on "Parasitic diseases of the eyes." Another was on "Retrolental fibroplasia"; a third, "Secondary glaucoma"; a fourth, "Trachoma"; and one on the "Effect of sunlight at high altitudes, the effect of bright light at sea level, and the problems of supersonic speeds."

There were four papers on "Military ophthalmology"; several symposia on "Industrial and school eye problems"; two on "Surgery of the eye and adnexa"; and a most interesting illustrated discussion on the subject of "Nematodes in children's eyes," given by Helenor Campbell Wilder. A summary of many of these papers was printed in two languages, in an attractive presessional volume, copies of which may be had for $1.50 each.

The last day of the meeting was devoted to research in ophthalmology. This part of the program was arranged by Dr. James H. Allen, who presided. Nine papers were presented on such subjects as "Average ocular tension," "Hyaluronidase," "The mechanism of foreign-protein therapy," "Microwave therapy," "Esotropia (statistical study)," "Toxoplasma," "Retinal metabolism," and "The treatment of leprous pannus."

But all was not work or lectures, or movies, for the members of the local committee outdid themselves in arranging for diversions. There was a most enjoyable watersports show at the outdoor swimming pool of the hotel, after a barbecue dinner in the garden; also a cocktail party at the beautiful Indian Creek Country Club. None of us will ever forget either of these enjoyable evenings.

In addition, the Mexican government sent two delightful movies of Mexico and many interesting posters, advertising their country. Also, Dr. Cepero of Havana, Cuba, brought his beautiful movies with sound effects, showing excerpts of several of his trips to those attractive countries which lie south of us.

The result of this meeting seems to be a considerable increase in the interest of ophthalmologists in their neighbors, even though a different language is used. And all of us resolved not to miss the coming congress in Mexico City, January 6 to 12, 1952.

Thomas D. Allen.

VETERANS ADMINISTRATION HOSPITALS

All physicians should be interested in the developments that have been taking place in the veterans hospitals since the end of the second world war. Vast sums of money are being spent for veterans' care and in the construction of many new hospitals. Yet, there are probably few doctors who know exactly what is being accomplished and doubtless no one is completely aware of what the future holds. This editorial will be confined to the ophthalmological aspects and particularly those pertaining to the St. Louis Medical Area which comprises the states of Missouri, Kansas, Arkansas, Louisiana, Oklahoma, Texas, Colorado, and New Mexico.

Shortly after the war the authorities decided that a division of the United States and its territories into 13 regions under the general control of Washington would constitute a serviceable organization for Veterans Administration. In each area a chief consultant in every division of medicine,

called the Branch Section Chief, was appointed, and over these was a director. These branch section chiefs were to act as advisors in their specialties for the veterans hospitals in their areas. There were appointed also to most hospitals consultants and attending physicians who were in the neighborhood of the hospital and available for frequent visits, it being customary in most places for the consultant to visit the hospital approximately once a week and for the attending physician twice a week, the frequency of the visits varying with the needs of the hospital. These physicians were in addition to a group who were not on a visit basis, but were either full- or part-time, or on a fee basis, by which is meant that they were paid for the individual examinations of patients.

At least one meeting of the branch section chiefs with other full-time medical officers of the veterans organization was held. Reports were given by those who had already visited the hospitals in their areas and general plans were outlined. The smaller area to which the writer was assigned at that time included Missouri, Kansas, Oklahoma, Arkansas, and the "panhandle" of Texas. By the time of the first round of visits the post-war plans for veterans hospitals were already in effect and in many places the ophthalmological staffs were adequate and functioning satisfactorily.

After about two years it was decided to appoint dean's committees from medical schools in the vicinities of veterans hospitals to serve as advisory bodies to the hospitals. This change virtually excluded the branch section chiefs from their direct advisory capacity in about two thirds of the hospitals. Since the most interest from the specialty standpoint, particularly in a small specialty such as ophthalmology, was centered in hospitals with close affiliations to medical schools and this left only the more isolated hospitals in which very little ophthalmology was practiced, the major part of the interest was taken away. In the writer's own case only three hospitals were left and the nearest was 300 miles from his home. At none of these three were there definite assignments of beds for ophthalmological patients and in one of them the ophthalmological treatment rooms were being used for desk space.

It is not to be gathered from this that the appointment of dean's committees was a mistake. In fact, it was a very sensible move and has been responsible for a closer affiliation between the schools and the hospitals and has resulted in better service to the patients and better teaching opportunities for medical students. It did, however, make the branch section chief's position one of little interest. The directing group in Washington was undoubtedly aware of the dissatisfaction of this group and recently has taken steps to reinstate to a considerable extent the advisory position of the branch section chiefs.

About this time it was deemed best to consolidate many of the areas, reducing the number to six. Because of the change in policy and the willingness of dean's committees to welcome the branch section chiefs, now called Area Consultants, the situation has again become one that makes these consultants feel that they are serving a real purpose and they will be more willing to make sacrifices to visit these hospitals and be of such service as they can.

In the St. Louis Medical Area there are 24 active veterans hospitals and 12 in process of construction, five to be opened this year. Obviously in as large a territory as the St. Louis Medical Area, which covers between one fifth and one fourth of the United States, it is not feasible for a physician who is not on a full-time basis with the Veterans Administration to make the rounds of all these hospitals frequently. Fully appreciating this, the veterans organization has permitted the appointment of sub-area consultants and this is being rapidly done throughout the country. Obviously, this will save much time and travel by the chief area consultant.

The writer has just returned from a visit to 12 of these hospitals which required 14

days. Some remarks resulting from these visits may give a picture of the present situation of ophthalmology in this division of medical care of veterans. These 12 hospitals were all in the states of Missouri, Oklahoma, Arkansas, Texas, and Louisiana, but are not all of the veterans hospitals in these states. Of the group visited, six have dean's committees as advisors and six do not. Those with dean's committees are in or near large cities and medical schools, hence have more ophthalmic activity. In every instance the consultants representing the medical schools were most coöperative and showed great interest in their duties in the veterans hospitals. In places where residents were in training, it was evident that the young men were having good opportunities for learning and were availing themselves of them. The number of residents in these hospitals varied from none to three. The services where residents were present were from one to three years in duration. The beds devoted to ophthalmology in the entire group varied from none to about 15, though there was always flexibility and more beds could be found if the need arose.

The warmth of welcome was no less in the hospitals where there was no medical school affiliation than in the others. Ophthalmology in the former varied from almost none in hospitals designated for tuberculosis and almost as little in the neuropsychiatric group, to the general hospitals where, in most cases, there was an active eye, ear, nose, and throat full-time physician. One obtained the impression that these units tended to be a little too self-sufficient and were less eager to welcome local consultants. Dean's committees seem to be important in preventing a self-sufficient family attitude in the hospital.

The hospitals themselves are well equipped and for the most part of modern construction, comparing favorably with private hospitals throughout the country. Administrative officers, managers, and directors of the medical service are in general of fine caliber and seem well qualified in their respective fields. Americans should be proud of the work that is being done for their diseased and disabled veterans.

Most of the hospitals are adequately staffed and reasonably full. But some readjustment within the services might permit sufficient space for the immediate future. A different viewpoint, however, is apparently held by the government because a great number of new hospitals, and very beautiful ones with everything modern and usually no less than 500 beds, are being built throughout the country. *The Journal of the American Medical Association* for March 18, 1950, states: "Twenty-six new Veterans Administration hospitals are scheduled for completion during the calendar year 1950. These projects will contain about 11,710 new hospital beds. . . ." In the St. Louis Medical Area there are completed (but as yet unoccupied), or building, or projected 12 new hospitals. Most of these are nearing completion. They stand as immense monuments along the highways of these states. In viewing all the new hospitals the question of staffing them becomes as baffling as from what source the patients are to be drawn. There may be implications back of all of this that we shall not be too happy to face in the years to come.

One other question comes to the mind of a visiting consultant and that is the acceptance of veterans for hospitalization who are not truly entitled to this care under the existing laws which state in effect that a patient to be eligible for hospitalization in a veterans hospital must either be suffering from a service-connected disability or have insufficient means for hospitalization. One cannot help but question the fidelity with which this government dictum is followed. It is true that veterans who do not claim service connection in their disabilities are required to sign a statement with regard to their financial status. But the impression is received that the veteran does not consider too seriously the implications of affixing his signature to this statement. No matter how good the intentions of hospital managers,

there may be much pressure brought to bear by local veterans organizations if the admission of a veteran for any reason is questioned. And veterans organizations, being as powerful as they are politically, are very hard to resist when they take a determined stand.

The observer cannot help but question the need of all of these new hospitals while the Army and Navy are closing hospitals because of lack of patients. This is probably due to several factors, primarily perhaps a lack of strategic position of the hospitals that are being closed. One wonders, however, whether the lack of complete integration of services might not be a factor. A good example of what can be done is the beautiful Navy hospital at Houston which is now occupied by the veterans and, under an able manager who understands coöperation with a local medical school, is making a fine use of this handsome group of buildings.

In conclusion, the thoughtful observer who has made careful examination of the facilities and conduct of the veterans hospitals, if the St. Louis Medical Area is any criterion, may well be pleased with what is being done for our war casualties.

Lawrence T. Post.

OBITUARY

JOSEPH WILLIAM CHARLES
(1868-1950)

Joseph William Charles was born February 9, 1868, in Boonville, Missouri. He died in Barnes Hospital, Saint Louis, February 10, 1950. He was the second son of the Rev. Benjamin Hines Charles, president of the old Presbyterian Synodical College of Boonville. His mother was Achsia Holmes. His great-great-grandfather, Shadrach Bond, was the first governor of Illinois. His brother, Benjamin Hines Charles, became an eminent attorney in Saint Louis.

At the age of 18 years, Dr. Charles received his A.B. degree from Westminster College. His M.D. degree was acquired about four years later from the Saint Louis Medical College. After a three-year preceptorship in ophthalmology, under Dr. M. Hayward Post, he studied for 22 months in the clinics and medical schools of Europe and London. The impressions of this experience remained with him throughout the rest of his life. He would relate that returning from this trip, he had only one dollar and four cents in his pocket, and owed 1,800 dollars. Shortly after this he started the practice of ophthalmology in Saint Louis and rapidly established himself as one of the outstanding ophthalmologists in the middle-west.

Dr. Charles was scrupulously honest and maintained the highest standards of social and medical ethics. During his long life, he held many positions of responsibility and honor. He was affiliated with both the medical schools of Washington and Saint Louis Universities. For eight years he was ophthalmic consultant on the Board of the Missouri School for the Blind. He was also on the staff of a number of the leading hospitals of the city, being especially active in St. Luke's Hospital and the Missouri Baptist Sanitarium, as it was then known.

Although never a prolific writer, there are some very excellent articles from his pen. Most of these were presented either before the old St. Louis Ophthalmological Society, or its successor, the Saint Louis Ophthalmic Society, or the American Ophthalmological Society. He served on the council of this latter organization from 1926 until 1930. Dr. Charles was also a member of the American Medical Association, the American College of Surgeons, the American Academy of Ophthalmology and Otolaryngology, and the Association for Research in Ophthalmology.

He spent most of his leisure at the Bellerive Country Club and at the University Club, where he lived for many years. He was a member of the Presbyterian Church.

In 1905, he was married to Laura Merrill, who died a few years later. On October 22, 1930, he was married to Elizabeth Dorothy

Dorsey, who was his faithful companion throughout his last long and trying illness. Much of the sparkle in his eyes during these last years must be attributed to her constant care.

His was a cheerful, optimistic disposition. Until the last, he looked forward to recovery, even while admitting that at the age of 81 years his life expectancy according to statistics, was reduced to zero.

Although his sphere of activity was much curtailed during the last few years of his life and even though he had retired from practice and given up his office some time before his death, his loss will be deeply felt by all who knew him.

M. Hayward Post.

CORRESPONDENCE

On ophthalmic signs and symbols

Editor,
American Journal of Ophthalmology:

Some subjects are intrinsically difficult, some become difficult as one gets deeper into them, and some have difficulties thrust upon them. One such subject is ophthalmic optics, especially geometric optics. I want to point out just a few of these unnecessary difficulties.

In some textbooks on ophthalmology and optics almost the whole Greek alphabet is employed in the formulas and derivations of formulas. The student has to struggle with a symbolism which is foreign to him. On the continent and especially during the days when Helmholtz and Gullstrand wrote their classic works, Greek was a required study in every continental high school. Every educated man had studied some Greek and knew at least the alphabet. But very few doctors study Greek nowadays. A few commonly used Greek letters are known by everybody but, when the entire Greek alphabet is employed, unnecessary difficulties are created.

Or to take another matter—the designation of the principal points of the eye or lens. Even the latest books on physiologic and ophthalmic optics denote these points by H and H′. Why do the authors use the letter H for the principal points? Simply because they copied from the German, without giving the matter any thought. In German the principal points are "haupt-punkte" (head points), and the H is the first letter of "haupt." In German, the letter H suggests what it stands for and makes sense, but not in English. Here the letter to use is P, the first letter of "principal." Moreover, whenever there are two related values to be represented by the same letter it is always easier to remember them when you use P_1 and P_2. The subscript "one" suggests another subscript "two." P and P′ for the first and second point are not so suggestive and are even confusing as "prime" itself means "first." When the first and second principal points of the eye are denoted as P_1 and P_2, they are far more easily remembered and correctly applied in conjunction with other symbols than when they are denoted by H and H′.

Or take the two nodal points which are so often represented by K and K′ for the same reason of thoughtlessly following the German. In German the nodal point is "knotenpunkt" (knot-point), and the letter K in German makes sense and reminds the reader what it stands for, but not in English where the designation should be N_1 and N_2. The use of the "prime" with a letter, for example, L′ or C′ is not always undesirable. I use it in some formulas, such as, $C' = C \sin^2 a$, where C′ is the cylinder power in an oblique meridian, C is the full power of the cylinder, and "a" is the angle between the axis of the cylinder and the oblique meridian. But one must give thought to the matter and choose symbols that are natural and appropriate.

Or take the simple formula for conjugate foci for lenses and mirrors. Almost every letter of the alphabet has been used to denote the object and image distance and hardly two books agree on the same letters. But one of the earliest formulas used and found in elementary books on physics is still

the best; that is, $1/p + 1/q = 1/f$. Small p is the object distance from the first principal point (or the pole of the mirror or refracting surface) q is the corresponding image distance from the second principal point, and f is the focal length. The distance "p" becomes associated with the principal point or pole as no other letter can.

One of the most important formulas for combining lenses or optical systems can be written as $D_c = D_1 + D_2 - D_1 D_2 e$, where D_c = the combined dioptric power, D_1 and D_2 stand for the dioptric power of the first and second lenses or systems respectively, and "e" is the equivalent thickness or distance.

I could mention many more illustrations, but the above will suffice to make my point. Some may say that the use of the proper letter, best abbreviation, or most suitable sign is of little importance. From experience based on years of teaching I can say that it is of great importance. It is amazing how much easier and more meaningful the subject becomes when presented in a manner and with a symbolism which the student can easily follow because it is familiar and grows naturally out of the subject matter.

Now is there a remedy? It seems to me that the Committee on Optics and Visual Physiology might take up this subject. Let the committee standardize the signs, symbols, conventions, and so forth and thus influence writers of books to use a common and a more natural optical language. This will help not only newcomers to ophthalmology but will make the subject more understandable to those already in the specialty.

(Signed) Joseph I. Pascal,
New York.

BOOK REVIEWS

PHYSIOLOGY OF THE EYE. VOLUME I. OPTICS. By Arthur Linksz, M.D., F.A.C.S. New York, Grune and Stratton, 1950. 334 pages, 137 figures, index. Price, $7.50.

Walter B. Lancaster in a laudatory foreword deservedly commends this original exposition of physiologic optics for its accuracy, clear thinking, interesting style, and excellent illustrations. A masterly presentation of the modern conceptions of the physics of light is followed by a lucid and leisurely discussion of the fundamentals of geometric optics. His ingenious demonstration of the principle of the Maddox rod should be part of every laboratory course, though in general clinical applications are deliberately only lightly touched. He pointedly stresses that the letters in optical formulas should be suggestive and used in a systematic and consistent manner. Most of the leading references, such as Duke-Elder, Southall, Emsley, and Cowan, show a distressing individualism in this respect. Our national societies would render a distinct service to teaching by promoting a sensible standardization. In this revision the English usage of separating sphere and cylinder by a solidus (/) should be considered, as it has the signal advantage of being available in all printing and typing.

The eye as an image-forming mechanism is fully discussed, presenting the best available optical and biologic data. The final conclusion, derived principally from the recent extensive X-ray studies of Stenström, is that the chance combination of the refractive components accounts for the average refractive error, though most frequently these variations are correlated to produce the norm of mild hyperopia. In pronounced ametropia, however, the essential factor is abnormality of axial length.

This good book supplements but does not supplant existing standard texts. A companion volume on applied clinical optics, written with the same verve and authority, is needed to popularize adequately the significant advances in modern practice.

James E. Lebensohn.

ATLAS DER AUGENKRANKHEITEN. By Rudolf Thiel. Stuttgart, Georg Thieme, Ed. 3, 1948. Distributed by Grune and Strat-

ton, Inc., New York. 225 pages, 634 illustrations, mostly colored, index. Price, $18.00.

The fifth edition of this well-known and valuable book is a worthy successor of the previous ones. Many new and beautiful illustrations have been added. It is difficult to discover any subject pertaining to the external diseases of the eye or to those of the retina, choroid, and optic nerve that are not described and illustrated. A knowledge of German is not essential, for the illustrations speak for themselves and are most useful for teaching, particularly. Kodachrome photographs of the illustrations are especially valuable for projection purposes in the classroom. The paper used and the printing of the illustrations are equal to the best examples of prewar German medical books.

Derrick Vail.

El Valor del Exámen Oftalmoscópico en los Hipertensos Arteriales. Una Guia Para el Internista. (The Value of the Ophthalmoscopic Examination in Arterial Hypertensions. A Guide for the Internist.) By Dr. Juan Manuel Vila Ortiz. 214 pages, stiff paper cover, 13 black and white illustrations. Published by Editorial Rosario S. A., 1949 (Rosario, Argentina.) Price, 25 pesos.

This well-written and well-printed volume, by a leading Argentine ophthalmologist, aims to do what its subtitle suggests namely to guide the internist in the use of ophthalmologic diagnosis. It is divided into eight chapters: generalities; ophthalmoscopic signs; the ophthalmoscopic pictures of arterial hypertension; classifications of arterial hypertension upon which are based ophthalmoscopic evidences; diagnostic value, prognosis, and therapeutic indication and control of the ophthalmoscopic examination in hypertensive diseases; clinical records; examination of the ocular fundus by the internist; conclusions. Individual attention, with references to the literature, is devoted to the various signs, diabetic uncertainties are carefully discussed, and directions are given as to the actual use of the ophthalmoscope by the internist. This volume, by the president of the Ophthalmological Society of the Litoral, should be very useful to the Spanish-speaking physician.

W. H. Crisp

Bulletin de la Société Belge d'Ophtalmologie. No. 90, Meeting of November 28, 1948.

Weekers and Weekers believe that iridencleisis is the best of the antiglaucomatous operations, claiming a 96 percent normalization of tension in chronic, 93 percent in subacute, and 85 percent in acute glaucoma. If the iridencleisis does not work, they favor nonperforating cyclodiathermy.

Weekers and Hintz discuss regulation of intraocular pressure following iridencleisis. Since there is such a close correlation between the curve of pressures in normal persons and the curve in those eyes which have been successfully controlled by surgery, they postulate that the means of regulation is not a mere mechanical one, but is under physiologic vasomotor and circulatory control.

De Jaeger and Bernolet present two cases of fissures of Descemet's membrane with edema of the cornea. The first they thought was on an infectious basis, and gave sulfanilamide. Analysis of the aqueous humor suggested a tuberculous infection. In the second case, the aqueous was cultured and showed five colonies of staphylococcus per cc. Both of the patients were young and in good health and had the affection in only one eye without any known reason. Local therapy was without effect. Both cases improved under calcium therapy.

Wibo, Borremans-Ponthiere, and Wibo discuss maternal rubeola and congenital malformations. Complications occur mostly in those cases in which the mother has had the infection during the first three months of pregnancy. Malformations are most evident

in the eye, ear, and heart. Cataract is especially prominent. The eye is generally small. The iris is atrophied and the pupil dilates with mydriatics only with difficulty. There are also often retinal pigmentary changes especially localized about the macular region.

The English believe in operation as soon as possible when the cataract is dense enough to cause an obscuration of vision, to prevent amblyopic nystagmus. The French, on the other hand, prefer temporization between 1 and 12 years. Some prefer repeated discissions and others linear extractions. Because of the severe effects of the disease, they advise education of the public, including immunization of young women upon exposure, use of convalescent serum, and in some cases therapeutic abortion.

Kluyskens presents electroencephalographic studies on the visual fields, and concludes that inversion of the fields (the field when taken with the test object moving outward being smaller than with test object moving inward) is important in studying several conditions, notably hysteria and other functional affections, and in differentiating between organic and nonorganic lesions.

Moers presents a case of a corneal plaque following the treatment of a corneal ulcer by penicillin ointment. Weekers states that the vehicle was the cause.

Weekers and Thibert state that the size and appearance of the bleb following an iridencleisis is not necessarily indicative of the amount of drainage. Low tensions are often attained with a very flat and apparently nonexistent bleb. They advocate incision ab externo with a cataract knife, and stress incarceration of the iris.

François studied aqueous veins after inclusion of the iris and found that they were less common than normal, being found in 52 percent of cases. With a flat cicatrix he found them in 72 percent, in a filtering cicatrix in 44 percent. When the angle is open, they are found in 88 percent of the cases with a flat cicatrix and 68 percent with a filtering cicatrix; when the angle is closed, only 55 percent in a flat cicatrix and 25 percent in a filtering cicatrix.

Mathieu and Weekers found aqueous veins in the following cases: 9 out of 10 in glaucoma not treated; 10 out of 11 in glaucoma treated by miotics; 10 out of 10 in glaucoma treated by nonperforating cyclodiathermy; 20 out of 20 in glaucoma without high intraocular pressure; and 7 out of 7 in aphakic eyes which had been operated on for cataract; but only 19 times out of 33 after iridencleisis. They draw attention to this low percentage and state that to interpret this difference makes further observation necessary.

Michiels studied the permeability of the blood-aqueous barrier by injections of intravenous gum arabic. He concluded that the movement of the gum arabic is similar to that of protein, and that a kinetic phenomenon explains the passage better than a secretion theory.

Fritz says that, in many cases instead of a penetrating corneal transplant with its attendant dangers, a nonpenetrating but very deep graft could be used. He advises the use of a binocular microscope during the surgery. He discusses the advantages of the peripheral square and rectangular corneal transplant as compared to the circular.

Moers discusses the treatment in a 34-year-old woman with an optic neuritis with penicillin, with very good results. The etiology of the disease was unknown. Appelmans and De Graeve discuss streptomycin and treatment of ocular manifestations of tuberculosis. They conclude that lack of cure was due either to insufficient treatment or streptomycin resistance of the bacteria.

Zanen devised an apparatus to show graphically the alternation of binocular function, and states that the rhythm is under control of factors which are obscure, that it is absent in foveal vision, and that it cannot be voluntarily changed.

Bennett W. Muir.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Ashton, Norman. **Injection of the retinal vascular system in the enucleated eye in diabetic retinopathy.** Brit. J. Ophth. **34**:38-41, Jan., 1950.

Many methods of demonstrating the retinal circulation by injection with various dyes and plastic materials have been described but it is felt that injection with India ink provides the best opportunity for photographing the circulation. The enucleated eye is not placed in formol but only the free end of the nerve is dipped in the solution for a few minutes. Then under a dissecting microscope, the nerve is cut across and the central vessels are easily seen. These are first irrigated with distilled water through a fine glass cannula attached to a pressure motor set at 10 pounds. This is followed by irrigation with 10 percent formol solution and then with the India ink. The eyeball is placed in formol for 12 hours and the retina removed and mounted in a glass sphere. Three photographs of a severe diabetic retinitis with thousands of microaneurysms are presented.

Morris Kaplan.

Rodger, F. C. **The pattern of the corneal innervation in rabbits.** Brit. J. Ophth. **34**:107-113, Feb., 1950.

Reports on investigations of the pattern of the corneal nerves in rabbits are presented. The nerve fibers form networks at three levels, one in the substantia propria, one under Bowman's membrane and one within the epithelium. The fibers of the intra-epithelial plexus do not end within the epithelial cells but between them. No specialized end-organs were found. None of the branches of the main stem anastomose. Examination of vitally stained specimens before fixation is necessary. Two types of nerve fibers were differentiated: one was beaded and had a smaller non-beaded, probably dendritic link, and a second had the beads masked.

Orwyn H. Ellis.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Azzolini, U., and Faldi, S. **The clinical importance of argyrosis of the cornea in industrial diseases.** Rassegna ital. d'ottal. **18**:316-322, Sept.-Oct., 1949.

Among workers in the silver industries the appearance of argyrosis of the cornea

is of great clinical value since its recognition warns of the possibility of deeper damage. The conjunctiva is usually equally involved with the cornea and frequently there is staining of the nails, skin and buccal mucous membrane. The discoloration of the cornea may be grayish-green, bluish or brownish-yellow, the latter when Descemet's membrane is involved. Frequently the pigmentation forms a band close to the limbus. Similar changes have been observed where silver has been given by mouth or intravenously. Three cases of industrial argyrosis of the eye are reported. Eugene M. Blake.

Focosi, M. **The action of influenza virus on the cornea.** Boll. d'ocul. **28**:577-588, Oct. 1949.

Rabbit corneas were scratched and inoculated with influenza virus (two strains) either by instillation of the virus into the conjunctival sac or by direct intracorneal injection. The latter never produced pathologic changes; thus, only instillations after scarification were used and more than one half of the corneas showed gray infiltrations along the scratch lines 48 to 72 hours after inoculation. These infiltrations grew to a diameter of less than one millimeter, forming an irregular rosary pattern along the scratch lines. The epithelium covering the infiltrations soon disintegrated. No conjunctival nor iris involvement was observed, and after 7 to 15 days, fine scars marked the area of scratch and inoculation. Passage of virus from cornea to cornea was not possible. Histologically changes similar to herpetic keratitis were found. (4 figures, 25 references.)

K. W. Ascher.

Mann, Ida. **Induction of an experimental tumor of the lens.** Tr. Ophth. Soc. U. Kingdom **67**:141-153, 1947.

Although mitosis occurs in the epithelium of the lens through life, carcinoma of the lens is unknown. Possible reasons for this are discussed. Experiments are described in which cancer of the lens was induced by chemical carcinogens in mice of pure-line strains. These demonstrate that the epithelium can become malignant and throws some light on the immunity of the lens in the body. (9 figures.) Beulah Cushman.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Auricchio, G. **Passage of glucose through the lens capsule after corneal paracentesis.** Boll. d'ocul. **28**:490-492, Aug., 1949.

In previous calculations, the author had used the equation of Fick which he now replaced by that of Davson and Quillian; a table shows the figures obtained.

K. W. Ascher.

Charamis, J. **Ocular allergy in handlers of streptomycin.** Brit. J. Ophth. **33**:714-715, Nov., 1949.

In Greece streptomycin is widely used in the treatment of tuberculosis and although toxic effects on the patients are rare, allergic manifestations in the handlers of the drug and in the doctors and nurses who administer it are very common. This allergy appears from one to six months after contact.

Morris Kaplan.

Dieter von Rom, G. **Are there means to protect the eyes against light?** Klin. Monatsbl. f. Augenh. **115**:227-231, 1949.

While many of the commercially available protective drops show very little ability to absorb ultraviolet light, it was found that a new preparation "Solan" which contains a sulfonamide absorbs ultraviolet rays. (1 figure, 2 curves, references.) Max Hirschfelder.

Hogan, M. J. **The preparation and sterilization of ophthalmic solutions.** California Med. 71:414-417, Dec., 1949.

Quaternary ammonium chloride is used both as a wetting and a sterilizing agent and is compatible with most ophthalmic drugs. Orwyn H. Ellis.

Johnson, G. M. **Toxic effects of tetraethylpyrophosphate. Report of a case.** J. Florida M. A. 36:417-419, Jan., 1950.

Tetraethylpyrophosphate, a new insecticide, is similar to diisopropyl fluorophosphate, which has been used in the treatment of glaucoma. It is readily absorbed through the skin, through the mucous membranes of the conjunctiva and intestinal tract, or by inhalation, and is dangerous and highly toxic to warm-blooded animals. The toxic symptoms are miosis, lowering of ocular tension, ciliary muscle spasm, abdominal cramps, vomiting, cardiospasm, complete auriculoventricular dissociation, constriction of bronchial muscles, and convulsive seizures. Immediate action should be taken in the treatment of the severe systemic poisoning because death can occur rapidly. F. H. Haessler.

Key, S. N., Jr., and Key, S. N. **Use of hyaluronidase in ophthalmology.** Texas St. J.M. 46:31-33, Jan., 1950.

Hyaluronidase is an ezyme that liquefies the tissue cement substance. It is used as an adjunct to novocaine in order to increase its penetration into the tissues. It has been used in lid akinesia. Useful features are the absence of ballooning of the tissues, and more prolonged and deeper anesthesia. Irwin E. Gaynon.

Marsico, V. **Effect of veritol on the pressure in the central retinal artery.** Boll. d'ocul. 28:541-554, Sept., 1949.

Beta - paraphenyl - isopropyl - methylamine, manufactured as "veritol," was used as sulphate in 3-percent solutions for instillations into the conjunctival sac and in 2-percent solutions for subconjunctival and parenteral injections. The pressure in the central retinal artery was measured according to Baillart's technique. Twenty individuals were observed before subcutaneous administration and at intervals of 10, 30 and 60 minutes and two hours thereafter. Twenty individuals received five instillations at 10 minute intervals, ten persons were observed before and after subconjunctival injection of two to three drops of the solution preceded by alipin anesthesia; and ten persons received subcutaneous injections of veritol. Both the diastolic and systolic retinal arterial pressures were always measured. Four tables and two graphs summarize the results. After any type of veritol administration there was a drop in the diastolic retinal arterial pressure which was pronounced half an hour after the administration and returned to pre-experimental levels two hours after the medication; the systolic retinal arterial pressure showed a similar course. Both the systolic and diastolic pressures in the brachial artery were elevated after the subcutaneous administration. (20 references.) K. W. Ascher.

Németh, Lewis. **Antihistamines in ophthalmology.** Brit. J. Ophth. 33:665-669, Nov., 1949.

Histamine is present in the tissue cells in the preformed state histidin, and is released as histamine as a result of the irritative action of the union of antigen and antibody in these cells. The released histamine causes the symptoms of allergy. If this histamine is neutralized or deactivated, which can be accomplished by cer tain phenol-ethers, the allergic symptoms are lessened or obviated. A number of

antihistamines have been produced synthetically. Most are non-toxic and serve very well in diseases such as urticaria, edema of Quincke, hay-fever, vasomotor rhinitis and pruritis. The Ciba preparation of antistine-privine was used as eye-drop instillations in a number of patients with ocular allergies with uniformly good results. In addition, this type of therapy often brings favorable results in episcleritis, iridocyclitis and uveitis of focal origin. Morris Kaplan.

Pirie, A. **The effect of hyaluronidase injection on the vitreous humour of the rabbit.** Brit. J. Ophth. **33**:678-684, Nov., 1949.

Very little is known of the production or the fate of hyaluronic acid, either in the eye or in other fluids and tissues in which it is found, such as synovial fluid, skin or Wharton's jelly. Meyer suggested in 1947, and it is borne out by the experiments described here, that in the vitreous, hyaluronic acid circulates, becomes disaggregated and is removed constantly through normal exit channels. Rabbits' eyes were injected with hyaluronidase and the animals watched for a year to note the changes on the vitreous. The techniques of preparing the hyaluronidase and of the tests are described. The eyes were watched with slitlamp and ophthalmoscope and, upon slaughter, the composition of the vitreous bodies was determined. It was concluded, as was expected, that the hyaluronidase caused a rapid disaggregation followed by a slow hydrolysis of the hyaluronic acid resulting in fluid vitreous. This state remained for about six weeks after which the vitreous humours showed normal aggregated hyaluronic acid. This does not show a possible reversibility of disaggregation in the clinically pathologic vitreous but it does show that normal hyaluronic acid appears in the vitreous during life.

Morris Kaplan.

Waters, J. W. **Electroretinography of experimental animals.** Brit. J. Ophth. **34**:1-15, Jan., 1950.

Electroretinography affords the only objective method of assessing retinal function in animals, and some results of studies by means of it, detailed descriptions of the apparatus, and methods of its use are presented. Normal guinea pigs, pigeons and normal and vitamin-A-deficient rabbits were used. A comfortable animal will remain quiet for an hour under nembutal. The studies included response to white light, to light of different wavelength, dark adaptation curves and responses in vitamin-A-deficient rabbits. The results were quite as expected. In the vitamin-A-deficient rabbits some lowering of retinal sensitivity occurred before changes could be seen with the slitlamp although maximum depression did not occur until changes were grossly visible. A single dose of vitamin A concentrate containing 10,000 I.U. was sufficient in some cases to restore the sensitivity to its original level. Morris Kaplan.

Zamorani, Giorgio. **Clinical and experimental data on the naso-retinal reflex.** Riv. oto-neuro-oftal. **24**:423-449, Sept.-Oct., 1949.

The naso-retinal reflex provoked either by a mechanical or by pharmacologic stimuli gives rise to changes in the retinal circulation. The retinal arterial pressure increases or decreases as the sympathetic or the parasympathetic nervous sympathetic system has been excited. Nicotinic acid on nasal mucous membrane always provokes a decrease of pressure, probably through excitation of the parasympathetic. Owing to the complexity of the naso-ocular neurovegetative innervations, the anatomic pathways have not yet been established; only a physiologic interpretation is possible. (References.)

Melchior Lombardo.

4
PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Betsch, A. **The refraction curve.** Klin. Monatsbl. f. Augenh. 115:205-213, 1949.

Variation curves of each of the optic media of the eye are binominal for each separate structure. The curve of refraction for the combined structures shows, however, a "positive excess" by being too high in its center and too broad at its base. In order to explain this problem two curves of refraction are construed by the author. In one group there exists a fixed correlation between corneal curvature and length of axis of the eye, in the second group various lengths of axis are assumed. Mathematical manipulation results in a typical binominal curve for each separate group. Whenever the two groups are combined and the number of eyes in the first group with fixed correlation is at least doubled as compared with the number in the second group, a total refraction curve is obtained which also shows the characteristic positive excess. (9 tables, 5 curves, references.) Max Hirschfelder.

Katz, Joachim. **Ametropia and visual acuity.** Klin. Monatsbl. f. Augenh. 115:197-200, 1949.

The smallest retinal area which sees two points as being separated from each other has a diameter of 10μ. One point corresponds, therefore, to one half of this amount, 5μ. This is the approximate size of one cone and corresponds to a visual angle of one arc minute. This is the smallest circle of dispersion in a normal emmetropic eye, variable in itself by width of pupil and wave length of the incoming rays. The circle of dispersion increases in the ametropic eye and the diameter of the retinal sector which sees two points as separate entities becomes larger. The author develops the mathematical formula needed to correlate the visual acuity of the ametropic eye with the visual acuity of one arc minute in the emmetropic eye.

Max Hirschfelder.

Martin, L. C., Day, D. J., and Kaniowski, W. **Visual acuity with brief stimuli.** Brit. J. Ophth. 34:89-104, Feb., 1950.

In these experiments the aim is to increase the intensity range beyond those of previous observations. Double-star and Foucault grating test objects are employed with both the dark-adaptation and low light-adaptation series recorded. The first reaction in scotopic vision is apparently the absorption of light by the chromophore groups of the rhodopsin or similar molecules thought to be associated with the protein layers in the outer segments of the retinal rods. The initial visual photochemical effect would be very short in comparison to the longer periods required for true photopic adaptation which may represent the reconstitution of chemically separated substances. The visual resolution is intimately related to intensity discrimination, since the aberrations of the optical system of the eye produce a degradation of the contrast of the retinal image which increases as details become smaller. The limiting angles were found to be small. The results did not suggest that eye movements have a major effect in increasing visual acuity. The effects of high intensity flashes were also studied.

Orwyn H. Ellis.

Mehlhose, F. **Transitory myopia after sulfonamide medication.** Klin. Monatsbl. f. Augenh. 115:217-227, 1949.

Transitory myopia after sulfonamide medication disappeared in two patients after instillation of atropine. This indicated that ciliary spasm was the cause. In a third patient atropine failed to reduce the myopia. The fact that normal breadth of accommodation persisted in this third patient after full correction of the myopic

condition makes it unlikely that edema of the lens is the cause of the condition. Sulfonamide myopia is probably an allergic reaction in people who have an idiosyncrasy to the drug. This reaction takes place in the brain and leads to small circumscribed areas of edema and hemorrhage. One of the author's patients also showed mild cerebral symptoms other than the ciliary spasm which caused transitory myopia. Sulfonamide myopia is like other transitory myopias after infectious diseases. It is not caused by toxic influences on the lens.

Max Hirschfelder.

Ohm, J. **The objective determination of visual acuity by means of optokinetic nystagmus in simulated blindness.** Klin. Monatsbl. f. Augenh. **115**:193-197, 1949.

The author describes the methods used in determining optokinetic nystagmus in a person who alleged blindness in his only eye. A rotating cylinder bears test marks of various sizes. The method not only enables the examiner to evaluate the actual visual acuity but to register the nystagmus graphically. (3 figures, references.)

Max Hirschfelder.

Schober, Herbert. **A simple accommodometer.** Klin. Monatsbl. f. Augenh. **115**: 214-216, 1949.

An instrument for determination of nearpoint and breadth of accommodation is described. Duane's figure, numerals and linear marks are used for test charts. Arrangement of the handle permits viewing of the test charts in a 45-degree downward position. A schedule indicating various areas of needed accommodation in different professions and occupations is given. (1 figure.) Max Hirschfelder.

Tyser, P. A., and Letchworth, T. W. **A study in visual defects in young children.** Brit. M. J. **2**:1022-1023, Nov. 5, 1949.

The authors describe a method of screening large groups of children of preschool age for refractive errors. In groups of 10, the children were examined by darkroom retinoscopy, without mydriatic drug. Any "against" movement of the red reflex, using a plain mirror, was noted as "myopia"; then a +2 diopter lens was held before each eye, and any "with" movement was classified as "hyperopia." These children were referred for further examination. About 8 percent of the 460 children examined showed a gross refractive error and 27 of these children were subsequently found to have a refractive error. One fourth of those screened out were already wearing glasses.

Benjamin Milder.

5

DIAGNOSIS AND THERAPY

Barrère, L. E., and Allen, J. H. **Prophylaxis of gonococcic ophthalmia neonatorum.** Arq. brasil de oftal. **12**:117-122, 1950.

The bacterial flora of 1618 eyes in 809 new-born was studied. The mothers of 288 of these children had received injections of penicillin during the 24 hours before birth, while 321 mothers had received no penicillin or other treatment. In 65 percent of the eyes there was no bacteriologic abnormality immediately after birth. The percentage was not modified appreciably by the antepartum injection of penicillin, but such injection did result in reduction of the development of Gram-positive and increase in the Gram-negative organisms.

W. H. Crisp.

Dahmann, F. **Local and general use of sulfonamides in eye diseases.** Klin. Monatsbl. f. Augenh. **115**:260-267, 1949.

Favorable results are reported from the topical application of the German sulfonamide preparations Badional, Supronal and Marbadal in various infectious conjunctival and corneal diseases, and also from

subconjunctival injection of a 7.5-percent sulfonamide solution in a severe case of serpent ulcer. Internal medication with a single large dose of sulfonamide supports these measures. Diseases of the posterior part of the eye and of the vitreous do not respond readily. Max Hirschfelder.

Duke-Elder, S., Ainslie, D., and Boase, A. J. **Aureomycin in ophthalmology. (A preliminary report)** Brit. J. Ophth. **34**: 30-37, Jan., 1950.

Aureomycin has been shown to inhibit the growth of a considerable number of organisms, notably staphylococcus, pneumococcus and H. influenzae, as well as the rickettsiae and a number of viruses and is particularly indicated in the treatment of organisms which are insensitive to penicillin. Although the amount of the drug available for this study was small, it was used orally and by instillations on a number of routine ophthalmic conditions in England, and in 8 cases of active virulent trachoma in the Uganda Territory of Africa. The results in England were fair while those in Uganda were most startling.

For systemic use 20 gms. of the drug were given orally as aureomycin hydrochloride in doses of 500 to 750 mgms. at 6-hour intervals with the topical instillation of 1 to 2 drops of solution at half-hour intervals. Eighteen patients were treated in England with no appreciable toxic effects; one with blepharitis was cured, one with influenzal conjunctivitis considerably improved and one with inclusion blenorrhea cured. Seventeen patients with corneal lesions, 12 with iridocyclitis and one with sympathetic ophthalmia were not benefited. The eight cases of active trachoma were treated with drops only and in each case the results were a complete cure in a few days. Even long standing pannus disappeared.

Morris Kaplan.

de Györffy, Istvan. **Therapeutic contact lenses from plastic.** Brit. J. Ophth. **34**:115-118, Feb., 1950.

Contact lenses can be used in many ways for therapy in close and prolonged contact with a diseased cornea. Desiccation and erosion can be prevented and treated. They may be used postoperatively in keratoplasty and ptosis. Ocular shells are used to prevent symblepharon after burns or surgical repair. Plastic moulding of shells for exact corneal impression have been found satisfactory.

Orwyn H. Ellis.

Halberg, G. P. **Organization of a photographic department.** Brit. J. Ophth. **34**: 121-125, Feb., 1950.

This report presents necessities for the organization of a complete photographic department. Particular mention is made of the electronic flash as a source of illumination and modifications of the Zeiss-Nordenson fundus camera.

Orwyn H. Ellis.

Halbron, P., Lepage, F., and Mawas, H. **An experiment in prophylaxis of ophthalmia neonatorum with penicillin.** (In French.) Arq. brasil. de oftal. **12**:123-125, 1950.

In a series of 4,000 cases, systematic instillation of a solution containing 5,000 units of penicillin per cc. in the eyes of the new-born was much more efficacious in prophylaxsis than the classic Credé method. W. H. Crisp.

Klein, M. **Contact shell applicator for use as a corneal bath.** Brit. J. Ophth. **33**: 716-717, Nov., 1949.

The author describes a modified contact lens which is used to give continued medicinal baths to the cornea. Attached to the corneal segment are two small studs that serve as a handle and have openings for the inflow of the drug and the escape of air. Morris Kaplan.

Nigro, Laetitia. **The diagnostic importance of retinic systolic arterial pressure.** Riv. oto-neuro-oftal. **24**:409-422, Sept.-Oct., 1949.

The unilateral lowering of systolic retinal arterial pressure is a sign of an endoarteritis of obliterant type. Primary thromboangiitis of Buerger can be suspected in the presence of occlusion of the central artery of the retina if the patient is not over 55 years of age, and if other etiologic factors can be excluded. An obstacle to the circulation of the subclavian artery (aneurysm, endoarteritis) causes a lowering of brachial systolic pressure and if the retinal arterial systolic pressure of the same side is normal the homolateral carotid is not involved. If the same condition is found on the right side it can be assumed that not only the carotid but the anonymous artery is also affected.

Melchior Lombardo.

Savory, Miss. **Some uses of thrombin and fibrinogen in ophthalmic surgery.** Tr. Ophth. Soc. U. Kingdom **67**:323-336, 1947.

Thrombin will produce rapid clotting of fibrinogen solution or of blood which contains fibrinogen. It may be valuable in ophthalmic surgery because of its adhesive quality in mucous membrane grafting and in conjunctival surgery as a plastic distending agent and as a hemostatic. In mucous membrane grafting, where the graft must be immoblized until its blood supply is established, fibrinogen solution is dropped on the bed and the graft is immediately placed and spread out into its final position. Clotting seems to take about one minute and after this the graft becomes adherent. Before dissection of the lacrymal sac methylene blue is injected to distend it.

Beulah Cushman.

Woods, A. C. **The use of antibiotics and sulfonamides in clinical ocular tuberculosis.** Tr. Am. Acad. Ophth. pp. 207-222, Jan.-Feb., 1950.

In 14 cases of ocular tuberculosis marked improvement followed treatment with streptomycin and promizole. Streptomycin was administered intramuscularly in doses of 0.5 gm. every 12 hours. Promizole was given orally, 6 gms. daily, in divided doses. The series included uveitis with concomitant scleritis, sclerokeratitis, diffuse scleritis and exudative choroiditis. The ocular disease conformed to the pattern regarded as tuberculous; the patients showed evidence of preceding ocular tuberculous infection; the cutaneous reaction was in conformity to the patient's age and tuberculous status; and thorough and exhaustive examination revealed no other apparent causative systemic disease to which the ocular inflammation could be attributed. Clinical improvement was noted after 9 to 21 days of treatment, and continued more slowly, but progressively. Reversible ocular changes regressed. Toxic symptoms developed after the therapeutic response and included vestibular irritation following streptomycin, and weakness and malaise from promizole. They were not serious, however, and promptly disappeared after the discontinuance of the drugs. Chas. A. Bahn.

6

OCULAR MOTILITY

Casari, Gianfranco. **Scotometric findings in dynamic strabismus.** Rassegna ital. d'ottal. **18**:338-365, Sept.-Oct., 1949.

Ten cases of concomitant strabismus, one of which was alternating, were studied with special attention to the presence of central scotomata, both before and after optic, orthoptic and surgical treatment. The scotomata were generally exactly central in the convergent eye, but at times paracentral and close to the normal blind spot. The scotoma was more extensive in binocular than monocular persons and

increased in size with decreasing visual acuity. The center of the scotoma was close to the fixation center and the size corresponded to the angle of deviation. In some cases the scotomata disappeared after treatment. The question of retinal correspondence assumed a prognostic value in the application of all phases of therapy. (10 figures, 2 tables.)

Eugene M. Blake.

Granstrom, K. O., and Magnusson, J. H. **Convergent strabismus, macular foci, and toxoplasmosis in monozygotic twins.** Brit. J. Ophth. **34**:105-107, Feb., 1950.

The authors present an interesting case report of monozygotic twins. The children developed almost identically and both had a right convergent strabismus. In the macula of each right eye there was an old chorio-retinal lesion. Tests for toxoplasmin were positive in the twins and parents, but negative in older siblings.

Orwyn H. Ellis.

Gutzeit, Richard. **Prism effect of decentrated lenses and their use in muscular imbalance and strabismus.** Klin. Monatsbl. f. Augenh. **115**:200-205, 1949.

Presbyopes with convergence insufficiency have difficulty with strong convex lenses, if they are not properly decentered. Prisms are frequently indicated. Decentration is sometimes useful in strabismus, to aid in binocular vision. However, even strong lenses very seldom yield enough prism power through decentration, especially in children who can wear only lenses of small size. While prism treatment is useful in the refractive types of strabismus, little or no value can be claimed for the muscular or innervational types, especially for divergent strabismus in hyperopes or convergent strabismus in myopes.

Max Hirschfelder.

Mellick, A. **Convergence deficiency.** Brit. J. Ophth., **34**:41-46, Jan., 1950.

In one year 88 patients presented themselves with convergence deficiency. They ranged in age from 14 to 50 years. Fifteen of the patients were unsuitable for orthoptic treatment because 12 had a very pronounced neurosis and three had a recent severe brain injury. Ten others failed to continue their treatment. Of the remaining 63, 48 or 76 percent were believed to be neurotic, in 6 the symptoms began after an acute illness and in 9 no apparent precipitating factor was evident.

In the neurotic group 37 were considered cured as a result of treatment, 4 were improved and 7 made no progress. The 6 patients in whom the deficiency followed an acute illness responded to treatment, while of the remaining 9, 5 were entirely relieved, 3 were improved and 1 was not benefited. Eighteen patients who had objective convergence deficiency complained of no symptoms and 29 who had appreciably more than the required 21 prism diopters complained of discomfort. Refractive error seemed to play no part in either of these groups but it was felt that most of the disturbances were purely functional. The question of why the neurotic subject should fix upon the ocular system for his psychosomatic manifestations remains to be answered.

Morris Kaplan.

7

CONJUNCTIVA, CORNEA, SCLERA

Ciotola, G. **Late results of corneal transplantation.** Boll. d'ocul. **28**:471-489, Aug. 1949.

Forty patients were followed for some months to three and a half years after corneal transplantation. While the final result can usually be judged after a few months, unexpected changes may occur later when the corneal disease relapses and the transplanted disc becomes involved. A graft performed for conical cornea remained clear for a year but be-

came involved in the same process of ectasia which had produced the original corneal disease. The concave spheric correction increased from 6 to 18 diopters within a year. One table summarizes the case reports, another shows the relation between etiology of the corneal disease and end result (best in eyes with inactive interstitial keratitis). A third table demonstrates the visual acuities obtained, (four times 10/10, and 12 times 5/10 or better) and the fourth table compares the end results reported by different authors. (33 references.) K. W. Ascher.

d'Ermo, F. **Clinical picture and etiology of primary corneal edema.** Boll. d'ocul. **28**: 529-540, Sept., 1949.

A 48-year-old woman had repeated attacks of unilateral or bilateral edema of the superficial corneal layers. No inflammation and no pressure increase accompanied these attacks, which coincided with increases of the blood histamine content. Antihistamine drugs (Neo-antergan) reduced the frequency, and the severity and the duration of the attacks.

K. W. Ascher.

Godtfredsen, Erik. **Relation between kerato-conjunctivitis sicca (Sjøgren's disease) dysphagia sideropenia (Plummer-Vinson syndrome) and ariboflavinosis.** Tr. Ophth. Soc. U. Kingdom **67**:175-183, 1947.

The Plummer-Vinson syndrome and ariboflavinosis are ascribed to defective cell oxidation. Sjøgren's syndrome has so many features in common with these two diseases that it is not unlikely that it too results from defective oxidation in the epithelial cell from another cause. The enzymatic nature of this oxidation is complex and vulnerable. Its occurrence in women in the menopause suggests that a hormonal disturbance may play a part.

The etiology of Sjøgren's syndrome is still obscure and its ophthalmologic treatment symptomatic. It should be emphasized that the Sjøgren syndrome should be sought for particularly in polyarthritic patients. Beulah Cushman.

Lack, A., Adolph, W., Ralston, W., Leiby, G., Winsor, T., and Griffith, G. **Biomicroscopy of conjunctival vessels in hypertension.** Am. Heart J. **38**:654-664, Nov., 1949.

Using a slitlamp, a microscope with magnification of 200 times and a movie camera, the authors studied the conjunctival capillaries in a series of 100 hypertensive patients. They found that in the hypertensives the capillaries showed extensive narrowing, tortuosity and fixed angularities with thickening of the capillary walls. A significant finding was a loss of normal capillary distensibility. In long standing hypertension a sparseness of the capillary bed was noted. The changes were well correlated with the height of the diastolic blood pressure.

In 96 of the patients studied, the authors found clumping of the red cells in the vessels. Apparently this phenomenon was not specific for hypertension because it was also found in two thirds of a series of nonhypertensive hospital patients, whereas only 2 percent of a normal controlled series was found to have intravascular clumping. The authors stressed the fact that the capillary abnormalities are consistently present in hypertension, and that on occasion significant vascular findings have been confined to the capillaries. Benjamin Milder.

Lepri, G. **Severe infection of the cornea with Proteus morganii.** Arch. di ottal. **52**: 231-255, Sept.-Oct., 1948.

In a case of severe traumatic infection of the cornea no improvement followed topical and systemic administration of penicillin and sulfonamides, but the eye improved rapidly on streptomycin and expansin. Bacteriologic studies and experi-

ments on animals showed that the infectious agent was a microörganism belonging to the proteus group. This is the first recorded case of an ocular infection with proteus morganii which is thought to be responsible for some cases of infantile gastroenteritis. F. Blodi.

Loewenstein, A. **Corneal blood staining.** Tr. Ophth. Soc. U. of Kingdom **67**: 155-168, 1947.

There is no census of opinion since Jacobson (1883) described the first case or since Hirschberg (1890) coined the name "hemorrhage into the cornea." Griffith (1894) introduced the name "blood staining of the cornea."

Hemorrhage into the anterior chamber generally precedes the condition. The hemorrhagic aqueous intrudes into the corneal parenchyma and it usually takes 10 to 14 days. The stained area may reach its full size on the first day. In the majority of cases, damage to the cornea is definite. On rare occasions, the corneal opacities get thinner and may even disappear. The fate of the eye usually depends on other factors.

The author reports five cases of which four were investigated anatomically. The frequent occurrence of raised intraocular pressure emphasized the importance of glaucoma. Atropine appears contraindicated in cases of corneal blood staining and repeated paracentesis is recommended. Beulah Cushman.

Roper-Hall, M. J., **Self-inflicted conjunctivitis.** Brit. J. Ophth. **34**:119-120, Feb., 1950.

These cases, seen in troops, appeared as simple acute bacterial conjunctivitis with repeated exacerbations and deterioration. Unit discipline was found to decrease the incidence. Chillie seeds placed in the upper fornix was the most popular method. Orwyn H. Ellis.

Sommerville-Large, L. B. **Self inflicted eye injuries.** Tr. Ophth Soc. U. Kingdom **67**:185-201, 1947.

The author reported 375 cases of self-inflicted injury in India. Injury was commonly carried out when on fatigue duty, in detention or when engaged in uncongenial physical work. The commonest irritants used were castor oil and jejuirity seeds. Other kernels and ground mepacrine tablets were also used.

The patients were relatively easy to spot. They seemed overwhelmed by their misery and were trying to find at least temporary escape.

They usually had pseudo-membranous conjunctivitis with a typical lesion of the bulbar conjunctiva and swelling of the preauricular gland. The whole lower lid might be adherent to the globe or adherent in one area. The pseudo-membrane could easily be peeled off the lid leaving a bleeding surface. It would then recur but its final disappearance took place in three or four days. The cornea was seldom involved. Even the presence of old trachoma had no effect on the healing process. Beulah Cushman.

Sorsby, A., and Burn, R. A. **Treatment of infected corneal ulcer by subconjunctival injection of penicillin in doses of 1,000,000 units.** Brit. J. Ophth. **34**:16-29, Jan., 1950.

It has been shown that adequate concentrations of penicillin can be obtained in the cornea and aqueous by subconjunctival injections and now it has been further proved that by increasing the dose the level of concentration is proportionately raised and persists longer. The addition of adrenalin further increases the concentration and the persistence. In this series doses of one million units of white crystalline penicillin were injected at 24-hours intervals with most satisfactory results. The injections were given in 30 consecutive cases of infected corneal ulcer

of which 25 presented hypopyon. Of 17 eyes that had been previously healthy, 14 responded promptly to penicillin and the three which did not respond within 24 hours all showed Gram negative bacilli and were given streptomycin. Only one required more than two injections. All regained satisfactory vision and mostly clear corneas. In 13 previously diseased eyes, the responses were almost as startling and satisfactory, and in most of them only two injections were necessary. Except for one that needed enucleation, the corneas, when healed, were no worse than they had been originally. The older methods of treating this disease with sulfonamids orally, heat cauterizations and carbolization are now entirely outmoded.

Morris Kaplan.

Thomas, J. W. T. **Donor material for corneal grafts.** Tr. Ophth. Soc. U. Kingdom **67**:301-311, 1947.

The author gives an account of methods of obtaining satisfactory donor material for corneal grafts from eyes enucleated during life or after death. It can also be obtained by taking the graft directly from the eye of a cadaver ten to twelve hours after death without removing the eye. The graft may then be kept in cold saline solution up to five hours without impairing its efficiency. Beulah Cushman.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Cannizzo, E. G. **Effect of penicillin on luetic uveitis.** Boll. d'ocul. **28**:555-562, Sept., 1949.

In four patients with uveitis who were given penicillin, the iritis healed in 10 days and did not relapse. A complicating optic neuritis healed in 15 days without loss of vision. K. W. Ascher.

Csillag, Francis. **Early post-operative detachment of the choroid.** Brit. J. Ophth. **33**:694-700, Nov., 1949.

Postoperative detachment of the choroid often follows operations for cataract, glaucoma, iridectomy, trephine, sclerectomy, and cyclodialysis and has been reported to occur in as many as 62 percent of cases. In the author's series it occurred much more commonly after cataract extraction in which a scleral flap was made, or after intracapsular extraction. During these procedures, the scleral spur is ruptured and the newly formed aqueous pours behind the detached ciliary body, accumulates behind the choroid and causes its detachment. This continues until the torn spur is healed. A conspicuous feature is a persistence of a shallow chamber which had previously been thought to be due to faulty wound healing but which is not necessarily so. The prognosis is good. The eye usually is normal in one or two weeks with no loss of function.

Morris Kaplan.

9

GLAUCOMA AND OCULAR TENSION

Dienstbier, E., Balik, J., and Kafka, H. **A contribution to the theory of the vascular origin of glaucoma.** Brit. J. Ophth. **34**:47-58, Jan., 1950.

It seems now, after 100 years of study, that primary glaucoma is not purely a local disease of the eye but rather an eye complication of some constitutional disturbance. The authors believe that ocular hypertension is intimately associated with a breakdown of the general circulatory system and fluid balance. This study involves the examination of glaucoma patients with special reference to the cardiovascular system and of the colloid osmotic pressure of the plasma proteins. The series included 97 patients of whom 74 had primary and 23 secondary glau-

coma. Degeneration of the cardiovascular system was much more evident than was to be expected in this age group. The cardiovascular findings showed that the patients with glaucoma more often suffer from hypertension and advanced sclerotic changes with all its consequences than others. These changes result in altered permeability of the capillaries and angiospasm within the eyeball. In secondary glaucoma these same etiologic factors are combined with a local abnormality.

Morris Kaplan.

Esente, I., and Faldi, S. **Headache produced by the injection of histamine with special reference to its occurrence in glaucoma.** Arch. di ottal. **52**:273-293, Sept.-Oct., 1948.

After intravenous injection of histamine the authors examined the blood pressure of the brachial artery and of the retinal arteries, the intraocular pressure, the onset and the duration of headache. The intraocular pressure did not change. The secondary rise in the blood pressure (general and retinal) after the initial drop was slower and less high in patients with chronic glaucoma. At the same time the headache was more severe and lasted longer. This is attributed to the lack of elasticity of the retinal arteries in glaucoma. A similar reaction was found in patients with atherosclerosis and to a lesser degree in patients with essential hypertony. The authors define their "index of retinal pressure" for histamine. It is high in normal individuals, medium in essential hypertony, and low in patients with glaucoma or atherosclerosis. F. Blodi.

Fenwick, G. De L. **A therapeutic step in chronic glaucoma.** Brit. J. Ophth. **33**: 688-693, Nov., 1949.

In about one fourth of cases of acute congestive glaucoma, a retrobulbar injection of 1.5 cc. of 4-percent novocaine containing 1 drop of 1:1,000 adrenalin to each cc. will temporarily reduce the tension and the congestion. Surgery can then be done on a quiet eye. The chief danger is retrobulbar hemorrhage, which occurred in one out of 160 injections. This can often be avoided by injecting slowly, but to insure safety a blunt needle containing a stylet is described. The stylet is kept in place until the needle is behind the eye, then the blunt needle only is used.

Morris Kaplan.

Fornaro, L. **Correlation between acute glaucoma attacks and some meteorologic factors.** Arch. di ottal. **52**:256-272, Sept.-Oct., 1948.

In the warmest and coldest months of the year attacks of acute glaucoma are more frequent when the temperature rises. In the other months there seems to be a correlation with the periods of rain.

F. Blodi.

Goldman, H. **Poiseuille's law applied to the aqueous veins.** Ophthalmologica **118**: 496-519 Oct.-Nov., 1949.

The flow of aqueous from the anterior chamber through the corneoscleral trabeculum into the canal of Schlemm and from there into the aqueous veins is treated mathematically, in accordance with the principles of hydrodynamics worked out by Poiseuille. The mathematical analysis concerns itself specifically with the situation that prevails during the determination of the outflow pressure after Goldmann and with the compression phenomena of aqueous veins described by Ascher. The analysis is hampered by the lack of actual measurements of some of the most essential factors, such as the minute volume of aqueous elimination and the viscosity of the contents of the lamellated vessels. Correlation of outflow pressure readings and gonioscopic findings is attempted in three cases of glaucoma. Peter C. Kronfeld.

Di Luca, G. **Early glaucoma diagnosis: preglaucoma or potential glaucoma.** Boll. d'ocul. **28**:589-613, Oct., 1949.

The provocative tests suggested by Bloomfield and Lambert, by Schmidt, and by Sugar were performed on 120 eyes of normal and of glaucomatous subjects and of relatives of glaucomatous patients. Sugar's test, consisting of a combination of Schmidt's drinking test with Bloomfield and Lambert's jugular compression and cold application test, was found positive in 80 percent of all glaucomatous eyes tested, and negative in all eyes with normal intraocular pressure. An enlarged Mariotte's scotoma was found in 75 percent of all glaucomatous eyes. In persons related to glaucoma patients, a diagnosis of potential or preglaucoma should be made if, in the absence of any prodromal signs, the provocative tests are positive; enlargement of the blind spot may follow later. In almost one fifth of the 19 family members of glaucoma patients, the provocative tests allowed this diagnosis of potential glaucoma. Three family trees, each comprising 3 to 5 generations, are reproduced. Three graphs show the effect of the drinking test, the cold-pressure test, and of their combination. Among six tables, one shows the effect of amyl nitrate inhalation in comparison to the tests named above, one the effect of caffeine administration on eye pressure of glaucomatous eyes, one the effect of provocative tests on glaucomatous eyes that have had surgical therapy, and one the responses to provocative tests in family members of glaucoma patients. (References.)

K. W. Ascher.

Matteucci, P., and Ligorio, A. **The results of iridectomy in acute glaucoma.** Rassegna ital. d'ottal. **18**:323-332, Sept.-Oct., 1949.

The authors report on 363 eyes in which iridectomy was done for acute glaucoma from 2 to 11 years previously. In the greater number of the cases, the intraocular pressure was normalized and the vision well preserved, but the visual fields gradually decreased from the periphery and progressively with the length of time. Various theories are suggested as to the cause of such field loss. In general, iridectomy is satisfactory and desirable. (2 figures.)

Eugene M. Blake.

Weekers, L. **The mode of action of antiglaucomatous operations.** Ophthalmologica **118**:564-574, Oct.-Nov., 1949.

Ocular hypertension is no longer considered to be the essence of the glaucomas. Different pathogenetic mechanisms underlie the various forms of glaucoma. In chronic "essential" glaucoma the disease is caused by a particular form of vascular disturbance which may involve the uvea, the retina or the optic nerve. Ocular hypertension is dependent upon localization of the vascular disease in the uvea; it is a common but not a constant manifestation of glaucoma. Antiglaucomatous treatment consists almost exclusively of measures intended to relieve the state of ocular hypertension, either by reducing the rate of intraocular fluid formation, or by removing obstacles blocking the intraocular fluid channels or by facilitating the fluid transfer out of the eye.

The mode of action of the iridectomy in acute glaucoma is complex and poorly understood. In unilaterally iridectomized rabbits the essayist found that intravenously administered fluorescein enters the aqueous of the iridectomized eye more slowly than the aqueous of the control eye. Histologically a certain degree of atrophy of the ciliary body was found in the iridectomized eyes.

The various forms of sclerectomy and of iris inclusion operation are intended to promote absorption of the intraocular fluid through the subconjunctival spaces. Clinical observation shows that these explanations apply only partially or are in-

accurate. The sclerectomy by itself is ineffective in chronic glaucoma. The tension-lowering effect of iridosclerectomies depends upon the iridectomy and is present even if the operative scar is not fistulous. The antiglaucomatous operations lower the ocular tension by modifying, directly or indirectly, the intraocular blood supply. In glaucoma the intraocular blood supply and the relationship between blood and aqueous have become disturbed in the direction of ocular hypertension. The antiglaucomatous operations change the intraocular blood supply in the direction of ocular hypotension. This concept is supported by experimental findings reported in detail in previous publications. A number of experimental procedures, such as massage or compression of the globe, pricking of the iris or ciliary body, subconjunctival injection of chemical irritants, have in common that they cause a primary transient elevation of ocular tension followed by a more lasting ocular hypotony. During the latter phase the uveal vessels are in a state of marked dilation. This sequence of events, increased tissue pressure followed by an abnormally low tissue pressure, occurs in tissues other than those of the eye, after various forms of trauma. The response of the eye to such traumas follows a general physiological rule. Antiglaucomatous operations are to be considered as well controlled, beneficial traumas which cause lasting hypotension. The iridencleisis deserves first place among the antiglaucomatous operations because it is the least mutilating and the most "hypotonizing" surgical procedure. The effect of surface cyclodiathermy upon rabbits is described in detail. Again, it is an operation which inflicts a well controlled but very effective trauma upon the ciliary body.

Peter C. Kronfeld.

Wolff, Eugene. **Schnabel's cavernous atrophy.** Tr. Ophth. Soc. U. Kingdom **67**:133-140, 1947.

The author discusses the theory which Schnabel introduced in 1885 that the cupping of the disc in glaucoma is due to the type of cavernous atrophy to which he first called attention. He held that minute cavities appeared in the nerve both in front and behind the lamina cribrosa. Those in front of the lamina enlarge and coalesce. Those behind the lamina collapse and then the lamina is drawn back by contracting glial tissue. Thus the whole glaucoma cup is produced.

The author feels that this type of atrophy is a classical example of what happens when the blood supply to a part or organ is gradually cut off. The more differentiated tissues which require more blood to keep them alive degenerate and disappear before the supporting tissues. The effect on the optic nerve is the result of progressive diminution in the blood supply. (5 figures.) Beulah Cushman.

11

RETINA AND VITREOUS

Ballantyne, A. J., and Michaelson, I. C. **Some aspects of disease affecting the retinal veins.** Tr. Ophth. Soc. U. Kingdom **67**:59-81, 1947.

The author emphasizes the main diseases affecting the retinal veins in contrast to those of the arteries. The chief conditions are venous obstruction, vasculitis retinae of young adults and diabetic retinopathy. In them one sees variation, dilatation or sheathing and abnormalities of capillary circulation evidenced by microaneurysms, hemorrhages, exudates or new vessel formation. The differential diagnosis is based for the most part on the grouping and development of these details. There are two factors which produce occlusion, primary sclerosis and phlebitis. Primary sclerotic changes in the vein wall may cause narrowing and finally occlusion of the vein lumen with or without a superimposed thrombus. Slowing of the circulation due to arterial disease and

narrowing is frequently associated with this phlebosclerosis. Infective phlebitis with thrombus formation is linked with those cases of vasculitis retinae of young adults which develop central venous obstruction.

The consequences of occlusion of the central vein are manifest both in the visible retinal veins and in the capillary system close to the venules. The consequences are the result of stasis and anoxemia of the wall of the vein. The visible veins become sheathed by a uniform pale line in places on either side of the blood column (pipe stem sheathing). The capillary disturbance is expressed ophthalmoscopically in the hemorrhage, microaneurysms, dilatation of capillary channels and soft exudates, which constitute the familiar picture of central venous obstruction. The microaneurysms of diabetes are situated in the macular region and not in the course of the larger retinal veins. The diabetic process causes a degree of venous stasis which reinforces the angiosclerotic factors. (23 figures.)

Beulah Cushman.

Bedell, A. J. **Medical ophthalmology.** Proc. Inst. Med. Chicago **17**:394-402, Nov. 15, 1949.

The fundus pictures in diabetes, hypertension, nephritis and papilledema are described. The duration, rather than the severity, of diabetes is the important factor in retinopathy. The typical diabetic picture of dilated veins, yellow-white exudates and pleomorphic hemorrhages is described. The ophthalmoscopic features of diabetes are detailed, with illustrative case histories, which include retinitis circinata and retinitis proliferans. In hypertension, the arterial changes progress from spasm to visibility of the vessel wall and atherosclerosis. Cotton-wool exudates, hemorrhages, and papilledema are described. The author mentions the three major retinal complications of hypertension: central retinal artery embolism, endarteritis and central retinal vein thrombosis. Nephritis produces retinal changes similar to hypertension, but there is more retinal edema and exudation. The latter forms a macular star figure in advanced cases. The difficulty of differentiating malignant hypertensive retinopathy from nephritis is brought out. The normal variations in the optic nerve head are described, and the changes in papilledema are discussed. No photographs accompany the published text of this address.

Benjamin Milder.

Black, G. W. **Some aspects of the treatment of simple detachment of the retina, including vital staining of the retina by methylene blue.** Tr. Ophth. Soc. U. Kingdom **67**:313-322, 1947.

The value of rest is illustrated by the fact that permanent reposition occurred in six of 80 patients by treatment with rest alone. In aphakic eyes in which the results of surgery are notoriously bad, cures have been obtained simply by rest and immobilization of the eye. Sclerectomy has been advocated to reduce the capacity of the globe, but its immediate effect may be obtained by diathermic scleral contracture. This assists both the evacuation of fluid and the approximation of the retinal layers.

The author also presented his investigation of the injection of methylene blue subretinally. The substance causes intense staining of the retina and rapidly reveals the extent of a detachment. It also acts as a mild sclerosing agent and may assist in obtaining firm union of the layers. Ten cases, all clinically unfavorable, have been treated by this method and in five the retina was replaced. (1 figure.)

Beulah Cushman.

Guist, Gustav. **The technique of operative closure of retinal holes at the posterior pole.** Klin. Monatsbl. f. Augenh. **115**: 232-240, 1949.

To destroy less functioning tissue in

the macular area than is usually the case after trepanation and the introduction of potassium hydroxide in the region of a macular hole, Guist developed the following technique. He opens the conjunctiva between the inferior and lateral rectus and introduces a Graefe knife between these two muscles, perforating the sclera in the region of the ora serrata, which has been previously determined by diascleral transillumination. Under direct observation with the electric ophthalmoscope the knife is pushed through the vitreous toward the macula. The knife makes one or more scratches at the bottom of the hole. This results in a macular hemorrhage and subsequent fibrinous adhesions, obliterating the hole and curing the detachment. The scars and subsequent central scotomatas are considerably smaller than with the older methods. Bedrest can be shorter, but has to be strict in order to prevent extension of the macular hemorrhage into the vitreous. The method is based on the author's previous attempts to close retinal holes diasclerally through the introduction of fibrin instead of chemicals, and on the observation that double perforations of the eye which lead to bleeding in the region of the retinal holes rarely develop detachments. The operation had considerable success in 18 patients of whom 16 had foveal holes.

Max Hirschfelder.

Juler, Frank. **An unusual form of retinal detachment (cystic) in children.** Tr. Ophth. Soc. U. Kingdom **67**:83-96, 1947.

The author presented three cases of retinal detachment in children which seem to form a definite group. The detachments were peripheral, non-progressive or very slowly progressive, and located in the lower part of the fundus of one or both eyes. Large oval tears which sometimes increased in number were associated with thinness and delicacy of the free portions of the membranes and with defective central visual acuity. The syndrome is ascribed with probability to a cystic degeneration of the retina on a developmental basis, although a hemorrhagic or inflammatory origin may also be considered. Prognosis and treatment also are discussed. (3 figures.)

Beulah Cushman.

De Leonibus, Fernando. **Macular changes in eyes operated upon for retinal detachment.** Rassegna ital. d'ottal. **18**:300-315, Sept.-Oct., 1949.

De Leonibus reports the ophthalmoscopic and functional changes in the macula in 175 cases of retinal detachment. In order to secure good visual acuity, it is of maximum importance that surgery be done as soon as possible after retinal separation occurs. After more than one month lapses, good vision is rarely attained. When the macular region has been detached, small, central or paracentral scotomata and a zone of metamorphopsia almost always remain. Ophthalmoscopically visible changes vary from simple pigmentary dystrophy to cystoid degeneration. An extensive review of the literature and reports of illustrative cases are included.

Eugene M. Blake.

Longhena, Luisa. **Late results of stellectomy in retinosis pigmentosa.** Boll. d'ocul. **28**:513-528, Sept., 1949.

Prolonged observation of six patients subjected to stellectomy some years previously suggested that the unfavourable side effects of this operation were barely compensated by visual improvements. Seven sets of visual fields demonstrate the final deterioration of those who did initially promise some improvement; some eyes became worse soon after the operation, which often led to Horner's syndrome, to muscular hypotony, hemiatrophy, inhibition of lacrimation and sweating, to hyperemia of face and lids and

conjunctiva, and to color changes in the iris. (References.) K. W. Ascher.

Mylius, Karl. **Bilateral spontaneous retinal detachment in neurodermitis disseminata.** Klin. Monatsbl. f. Augenh. **115**: 247-250, 1949.

Neurodermitis and cataract is a well established entity. The connection between this skin disease and retinal detachment, on the other hand, is very unusual. The author observed two persons with bilateral detachment in whom the occurrence of retinal separation followed exacerbation of the skin condition. He speculates on a possible common cause through vasomotor disturbances and abnormal reaction of the sympathetic nervous system. Max Hirschfelder.

Rychener, R. O. **Retrolental fibroplasia.** Illinois M. J. **96**:299-302, Nov., 1949.

The author presents a brief review of retrolental fibroplasia from its first description by T. L. Terry in 1942, to the recent observations of Owens and Owens. The typical clinical picture is described, as found in premature infants. Statistical studies indicate an incidence of 12 percent in prematures weighing less than 3 lbs. at birth. Attempts have been made to correlate the incidence of the disease with other factors. The incidence in primiparous women was only half of that in multiparous women. Two cases are reported. Benjamin Milder.

Scholtyssek, H. **Rare ocular disease in myeloid leukemia.** Klin. Monatsbl. f. Augenh. **115**:251-255, 1949.

A patient had a thrombosis of the central retinal vein in one eye which was followed by glaucoma and fundus hemorrhages in the other eye. The first eye became irritated 18 months later and a grayish exudate consisting of red and white blood corpuscles was found in the anterior chamber. Myeloid leukemia was found at that time. The author points out that fundus hemorrhages, papilledema and venous thrombosis can be forerunners of leukemia, long before the typical leukemic retinopathy appears. The histologic findings in this case consisted of leucocytic infiltration in the uvea and dilation of the blood vessels with stasis. (2 figures in color, references.) Max Hirschfelder.

Streissle, K. **The pathology of closure of the central retinal vein in young persons.** Klin. Monatsbl. f. Augenh. **115**:255-260, 1949.

The eye of a 17-year-old girl with the clinical picture of thrombosis of the central retinal vein was enucleated because of subsequent iritis and secondary glaucoma. Great proliferation of the endothelial and subendothelial cells of the vein was found within the region of the lamina cribrosa. The artery was normal. The author points out that prognostically favorable cases are caused by spasm and momentary compression by surrounding edematous tissues without actual changes in the vessels. Repeated or continued ischemia may however lead to endarteritis and endophlebitis. Similar vascular changes are brought about by infectious processes in other parts of the body and caused most of the cases of juvenile thrombosis which were examined histologically. (1 figure, references.) Max Hirschfelder.

Vetter, Joachim. **The origin of retinal detachment.** Klin. Monatsbl. f. Augenh. **115**:240-247, 1949.

Occurrence of retinal detachment in several members of a family suggests an inherited disposition in certain cases. Reports from the literature as well as the author's personal experiences indicate that the detachment occurs earlier in life in the second generation than in the first. There are indications that poor local or general development of the glial connective tissue within the retina is a pre-

disposing factor in these cases of familial occurrence. Formation of holes is favored by this insufficiency of glial tissue. (1 family tree, references.)

Max Hirschfelder.

12

OPTIC NERVE AND CHIASM

Neame, Humphrey. **Congenital hole at the optic disc. Report of ten cases and special reference to visual field defects.** Tr. Ophth. Soc. U. Kingdom **67**:109-132, 1947.

The author found a visual field defect in the upper part of the central and paracentral region of the visual field several years after the hole in the optic disc had been noted. This suggested the visual field examination in succeeding cases. Definite defects of considerable size were found in four of ten cases and five of the remaining six had an enlarged blind spot. (15 figures.) Beulah Cushman.

Robson, J. T., and Cameron, W. **Optic neuritis from cold permanent wave.** Northwest Med. **48**:701-702, Oct., 1949.

Toxic reactions to thioglycolic acid are recorded, especially contact dermatitis. Case reports of mother and daughter with bilateral optic neuritis are presented. Bilateral edema of the discs with permanent visual loss followed the repeated use of the cold wave method. Response to treatment has been poor. No other etiologic agents were found. Orwyn H. Ellis.

13

NEURO-OPHTHALMOLOGY

Gomes Sobrinho, J. P. **A case of voluntary nystagmus.** Arq. brasil de oftal. **12**: 126-127, 1950.

The patient, a man of 30 years, stated that he had had meningitis in childhood. While his interpupillary distance was being measured he showed a nystagmus which diminished as he reduced his effort at fixation. The hearing was good, and laboratory tests showed nothing of importance. There was no spasm of accommodation, but production of the nystagmus could be repeated at will.

W. H. Crisp.

Raiford, M. B. **Optochiasmatic arachnoiditis; report of a case.** Virginia M. Mo. **76**:586-588, Nov., 1949.

The characteristic features of optochiasmatic arachnoiditis are described, including the rapid visual loss and ultimate optic atrophy, the concentric contraction of the visual fields and the radiologic evidences of deformity in the cisterna basalis by air study. The author reports the case of an eight-year-old boy whose vision was 2/60 in each eye. He had symmetrical contraction of both fields. There were no other neurologic findings but on the basis of the X-ray evidence a craniotomy was performed and adhesions about the optic nerves were freed. Benjamin Milder.

Spadavecchia, Vitangelo. **Naso-ciliary neuritis.** Riv. oto-neuro-oftal. **24**:389-408, Sept.-Oct., 1949.

Two cases are reported. One of true nasociliary neuritis occurred in a woman, 71 years of age, and was characterized by nervous irritative crises which alternated with neurogenic keratitis and iritis. The other, a degenerative parenchymatous neuritis in a boy, 13 years of age, is the first case reported with this name, and is characterized by corneoconjunctival hypoesthesia and hypoesthesia of the corresponding pituitary membrane, infrequent winking, keratitis of neuroparalytic type, incomplete Horner's syndrome, slight pain on pressure over the external nasal nerve and paresthesia.

Melchior Lombardo.

14

EYEBALL, ORBIT, SINUSES

Kilner, T. P. **The contracted socket.** Tr. Ophth. Soc. U. Kingdom **67**:275-279, 1947.

The author described his treatment in three groups of cases: 1. the pensioner fitted with an artificial eye (1914-1918) and returned between the two wars because "something had gone wrong" with his socket and he could no longer retain the eye; 2. an infantile socket, in which the eye was removed in childhood and the socket would only accept a diminutive prosthesis; and 3. sockets reduced in size and with actual loss of conjunctiva after trauma. (13 figures.) Beulah Cushman.

Lindeke, H. I., and Maiden, S. D. **Oculoglandular tularemia treated with aureomycin.** J.A.M.A. **142**:99-100, Jan. 14, 1950.

A case of oculoglandular tularemia is presented. There was a dramatic response to aureomycin which was continued for three weeks systemically and 15 days locally. Irwin E. Gaynon.

Marshall, J., Howells, A. H., Melanowski, W. H.; and Rycroft, B. W. **Rhinology in relation to ophthalmology.** Tr. Ophth. Soc. U. Kingdom, **67**:19-57, 1947.

The rhinologist and ophthalmologist should discuss the features of the borderland between their respective spheres at intervals with the aid of a radiologist to bring out the common problems.

This discussion was limited to the cause of reflex irritation of the external eye as a site of onset of orbital inflammation and of neoplasms involving the orbit and the ophthalmic nerves; the relation to sinus operations and disturbances of the eye and its adnexa; and dacryocystorhinostomy. Beulah Cushman.

Montresor, Dante. **A case of cranio-orbital colesteatoma.** Riv. oto-neuro-oftal. **24**:381-388, Sept.-Oct., 1949.

A girl, 17 years of age, had a nonreducible nonpulsating direct exophthalmos on the left side. The supraciliary region was slightly displaced upward and her left palpebral aperture was slightly wider than the right. Palpation revealed a soft mass which was adherent to the roof of the orbit. Transfrontal exploration showed an extradural cyst containing a mass of degenerated cells and cholesterol crystals which had eroded the lateral wall and some of the roof of the orbit. The histologic examination demonstrated a typical colesteatoma. The diagnosis of this rare cranial tumor is discussed. (4 figures.) Melchior Lombardo.

Stallard, H. B. **The contracted socket.** Tr. Ophth. Soc. U. Kingdom **67**:280-299, 1947.

Contracted sockets which may be associated with symblepharon may be the result of a shelving lower fornix with ectropion, a retracted socket floor after orbital cellulitis, organized hemorrhage or loss of the orbital fat, maldevelopment of the orbital walls and generalized contraction of the conjunctiva. Reconstructive treatment consists of the mechanical enlargement of the socket, division of symblepharon divided by a diathermy knife, and closing the opening by undermining the adjacent tissues, or use of buccal mucous membrane grafts. A thin epidermal graft is recommended for total lining of the socket. Adrenalin in saline or novocaine is injected beneath the conjunctiva of the floor and the fornices. Bands of fibrous tissue in the socket floor are dissected out, an external canthotomy is done, the conjunctiva is undermined as far as the plica and beneath the fornices. Care is taken not to interfere with the insertion of the levator of the lid. The lower fornix is deepened down to the periosteum of the floor of the orbit by introducing the closed blades of blunt-ended scissors and spreading the blades, for it is important to make the graft adhere to the periosteum of the orbital floor. Absolute hemostasis is necessary. The graft is inserted into the socket on a mould. The tarsorrhaphy and canthotomy sutures are tied. Then an even pressure bandage is applied.

Beulah Cushman.

15

EYELIDS, LACRIMAL APPARATUS

Morgan, O. G. **Stenosis of the lower canaliculus.** Brit. J. Ophth. **34**:113-114, Feb., 1950.

Stenosis of the lower canaliculus with epiphora may be operated upon by one of two methods. In the first a probe is passed through the upper punctum, the upper canaliculus is slit throughout its whole length and a tampon is inserted into its lower open end. If this slit remains open, the epiphora is controlled. In the other procedure a probe is passed from the sac into the lower canaliculus while performing a dacryocystorhinostomy and the lid is incised where the probe bulges. The probe is left in place for one week and the opening remains patent.

Orwyn H. Ellis.

Riddell, W. J. B. **Streptothrix colonies in the lacrimal canaliculus: report of a case, with a note on diffraction spectrum examination.** Glasgow M.J. **30**:452-454, Dec., 1949.

A case of streptothrix, the concretions of which occluded the lower canaliculus, is presented. Diffraction spectrum examination (X-ray) failed to reveal any calcium carbonate in the concretions.

Irwin E. Gaynon.

Toselli, Carlo. **Plasmoma of the lacrimal sac.** Rassegna ital. d'ottal. **18**:333-337, Sept.-Oct., 1949.

Because of epiphora and an elastic induration, the lacrimal sac was removed from a 55-year-old man. Physical, laboratory and X-ray studies were negative. The tissues of the sac were almost totally obliterated. Only traces of epithelial cells remained. The mass was composed almost exclusively of plasma cells. There were plasma and lymphocytic cells about and inside the vessels. Hyalin degeneration of the connective tissue was seen in the periphery. Eugene M. Blake.

Tough, T. S. **Some aspects of lid and socket repair.** Tr. Ophth. Soc. U. Kingdom **67**:203-219, 1947.

In old lacerations with distortion of the lid it is best to wait two or three months provided there is no risk to the eyes. All fibrous tissue must be excised and absolute hemostasis, by pressure, and the applications of thrombin, is necessary. The position of the canthi must be established and the lid margin repaired. If there is gross injury to the medial canthus, the tissues must be sutured with stainless steel to the periosteum of the lacrimal crest. If the suture line is long and vertical, it should be broken by interdigitating flaps. To fill in defects the rotation flaps of Blaskovics and More are best. For cicatricial ectropion, a Thiersch graft applied on a stent mould is used. The Wheeler graft from the upper lid to the lower lid gives an excellent match both as to color and texture. In contracted sockets the author preserves what conjunctiva there is. The graft is applied on an acrylic mould.

Glasses with toric or tinted lenses on the affected side are of cosmetic value. (35 figures.) Beulah Cushman.

Traquair, H. M. **Classification of epiphora with remarks on diagnosis and treatment.** Tr. Ophth. Soc. U. Kingdom **67**:169-174, 1947.

When the lacrimal apparatus is healthy, the excess secretion may be due to hypersensitivity to stimuli, and a thorough examination is required to discover such stimuli as uncorrected astigmatism, small conjunctival infarcts or misplaced eyelashes. Protection from wind and cold and mild astringents may do some good. Regurgitation on pressure on the sac characterizes disease of the lacrimal apparatus whether a stricture is present or not.

Among adults, the patients are predominantly women, and frequently there is a history of familial occurrence. Among infants, uninfected cases are rare.

Cases associated with disease of the lacrimal apparatus are best treated by drainage operation into the nose. Unless the canaliculi are free, intranasal drainage will not be satisfactory. Dacryocystitis in the infant should be treated by frequent expression a few weeks before probing. Probing should be done through the upper punctum and care must be taken to avoid making a false passage. Syringing should be done with great care. Slitting of the canaliculus is rarely of value.

Beulah Cushman.

16

TUMORS

Graff, P. W. **Cancerous melanoblastoma of the eye with visceral metastases.** Illinois M.J. 96:387-390, Dec., 1949.

A 62-year-old white woman died one year after enucleation of her left eye for melanoblastoma. Necropsy findings showed extensive metastasis to the liver, biliary lymph nodes and skin.

Irwin E. Gaynon.

Hutner, L. M. **Death from metastatic melanoma thirty-six years after removal of probable primary ocular tumor.** California Med. 71:420-421, Dec., 1949.

The patient had an enucleation 36 years previously, presumably for malignant melanoma, a simple mastectomy 10 years later with the pathologic diagnosis of melanoma and when seen in 1947 showed metastasis to chest and neck glands. The following year the patient died with generalized metastasis. Metastasis from malignant melanoma are generally widespread; however, they may remain dormant in the liver for 10 to 20 years.

Orwyn H. Ellis.

Michaelson, I. C., and Hill, J. **von Hippel-Lindau disease.** Brit. J. Ophth. 33:657-664, Nov., 1949.

The eye of a 24-year-old man with von Hippel's disease and typical signs of intracranial tumor was enucleated, and five days later a cerebellar hemangioblastoma was removed. Recovery was uneventful. Pathologic study revealed complete degeneration of the retina which consisted mostly of coarse bands of neuroglia through its whole thickness. There were many cysts of varying size, some empty and some filled. Clumps of pigment cells and pseudomembranes were found throughout but most striking were nodules of varying size situated in all retinal layers. These nodules varied from tiny clumps of cells to large hyalinated masses and seemed to be the essential lesion. In the brain, there were no nodules and no cysts but the tumor consisted largely of a matrix of endothelial tissue containing large blood channels.

The findings suggest that the endothelialization is primary and the overgrowth of neuroglia and the cyst formation are secondary. (9 figures.)

Morris Kaplan.

Saebo, Johan. **Primary tumor of the optic nerve.** Brit. J. Ophth. 33:701-708, Nov., 1949.

Primary tumors of the optic nerve are exceedingly rare and have been estimated to occur in from 1 to 25,000 patients to 1 to 198,000 patients. About 350 have been reported, to which number a case is added. A 45-year-old woman complained of reduction of vision in the left eye along with noticeable protrusion, but without pain or diplopia. The entire body was normal except for the left eye which presented proptosis, amaurosis, disc edema of 9 diopters, retinal hemorrhages and tortuosity of vessels. X-ray films were normal. Five months later the eye was more proptosed, red and painful, and X-ray films showed

a widening of the optic foramen. Intraocular pressure was elevated and the eye was removed for suspected tumor of the optic nerve. Intracranial surgery was recommended but refused and the patient died one year later of intracranial metastasis. Pathologic examination revealed a tumor of the nerve extending backward and consisting of a very highly cellular tissue which seemed to be primarily glial. It contained many immature cells in various stages of mitosis.

Morris Kaplan.

17

INJURIES

Thomson, A. M. Wright. **Vascular disturbances in the eye following concussion injuries.** Tr. Ophth. Soc. U. Kingdom **67**: 245-253, 1947.

The author called attention to the constriction of the retinal vessels in injuries to the orbit in 1941 and now reports several cases. Both inferior temporal arteries were constricted after a shot through both orbits. In three other cases extensive fibrous tissue formed in the retina at the site of the choroidal hemorrhages after a rifle bullet had traversed both orbits. The causes of vascular constriction are organic obstruction in the artery or vein, death of the retina after injury to the underlying choroid, and spasm as the result of an axon reflex. Axon reflexes play a big part in the appearances of the retina after concussion injuries of the choroid. (7 figures.) Beulah Cushman.

18

SYSTEMIC DISEASE AND PARASITES

Dérer, J., and Adda, V. **Internal ophthalmomyiasis.** Bratislavské Lekárske Listy **29**:1123-1128, 1949.

This case occurred in a 5-year-old boy. The grub was surgically removed from the anterior chamber and was identified as sarcophaga. The acute suppurative uveitis terminated with atrophy of the eyeball. The authors believe that the grub penetrated the globe through the cornea or sclera, although they concede the occasional possibility of entrance through the blood stream. The usual appearance of the disease in the winter season, and the fact that the fly lives only in the warm summer months, suggest that entrance into the body occurs months before actual involvement of the eye. W. H. Crisp.

Lindsay-Rea, R. **A case of Reiter's disease.** Tr. Ophth. Soc. U. Kingdom **67**: 241-244, 1947.

Reiter described a disease in 1916 characterized by polyarthritis, urethritis and conjunctivitis of unknown etiology. He believed a spirochete was responsible.

A young man, who had had a urethral discharge for 28 days and perianal abscesses four months before had a mucopurulent discharge from each eye. Culture from the urine showed a nonhemolytic streptococcus. Various joints became swollen the following month, and vision was reduced by iritis. Sulphonamides were given and the joints and vision became practically normal in one month.

Beulah Cushman.

Melanowski, W. H. **Cysticerosis of the eye.** Tr. Ophth. Soc. U. Kingdom **67**:229-239, 1947.

The author describes patients in whom cysticercus had been removed surgically from the eyelids, conjunctiva, anterior chamber, under the retina and in the vitreous body during his 26 years in Warsaw. (5 figures.) Beulah Cushman.

Walsh, F. B., Hogan, M. J., and Sabin, A. B. **Symposium on toxoplasmosis.** Tr. Am. Acad. Ophth. pp. 177-204, Jan.-Feb., 1950.

Walsh, F. B. Introduction of subject. pp. 177-182.

Following a historical review, the author discusses the pathology of the acute, subacute and chronic stages of toxoplasmosis. The principal symptoms and signs are: convulsions, hydrocephalus, mental deficiency, cerebral calcification and chorioretinitis. The diagnostic triad, however, is convulsions, cerebral calcification and chorioretinitis. If these occur in infancy, a diagnosis of toxoplasmosis is justified in 9 out of 10 cases. If chorioretinitis is not associated with cerebral calcification, the probability of toxoplasmosis is only 1 in 10. The characteristic histopathologic lesion is the microglial nodule. Discrete or diffused calcification usually occurs within scattered zones of necrosis. Organisms may often be obtained from the ventricular fluid which has a high protein content. Increase or decrease in the size of the cranium with evidences of increased intracranial pressure and calcification are the most frequent features observed radiographically. Hydrocephalus is readily demonstrable by air injection into the ventricular or spinal fluid from which toxoplasma may be isolated. In the differential diagnosis, tuberselerosis, subdural hematoma and retrolental fibroplasia are discussed. One tenth of the normal population apparently has neutralizing toxoplasma antibodies which suggests that mild cases are more frequent than is generally believed.

Hogan, M. J. Ocular manifestations. pp. 183-189.

Toxoplasma is a protozoan parasite from 4 to 7μ long and 2 to 4μ in breadth, which possesses distinct cytoplasm and nuclear chromatin. It has been observed within the cells of the reticulo-endothelial system, mononuclear phagocytes, and parenchymal cells, but may be free in the tissues. The parasite cannot be propagated in artificial media. Transmission may occur through food ingestion and vectors. The central nervous system, especially in the developing fetus, has a marked predilection for the disease. The earlier the prenatal ocular involvement, the greater, the ocular damage. Fetal infection usually occurs in later months of pregnancy. Of approximately 78 cases of congenital positive or probable toxoplasmosis with associated chorioretinitis, 33 had macular lesions only; 34 multiple lesions involving the macula and other portions of the fundus; the remainder, nonmacular lesions. The most frequent primary lesion is macular and binocular. The choroid is usually involved secondarily. Associated symptoms may be: nystagmus, ocular deviations, microphthalmus, uveitis, secondary cataract, vitreous opacities, optic atrophy, and papilledema due to an associated hydrocephalus. The posterior part of the eye is most frequently affected. The author describes the histopathology of the acute, chronic and healed stages. Mothers of toxoplasmic children usually show no signs of the disease during pregnancy. It is therefore probable that mothers harbor the parasites in an innocuous form and that infection of the fetus occurs during pregnancy through the placental circulation.

Sabin, A. B. Diagnosis and treatment. pp. 190-204.

There is little or no evidence that ocular lesions occur from a postnatal toxoplasmic infection, nor that healed chorioretinitis with arrested congenital toxoplasmic infection becomes active. The antibody neutralization or rabbit skin test which has been the principal serologic diagnostic criterion of toxoplasmosis is not considered accurate. A negative test does not indicate the absence of antibodies nor infection. A positive test does not differentiate between titers of doubtful significance. The more recent methylene blue dye test is considered much simpler and more accurate. It is based on the fact that

toxoplasma incubated with fresh immune serum remains unstained in alkaline methylene blue. The dye test titer refers to the highest original dilution of a serum which in the presence of a constant adequate amount of accessory factor is capable of depriving the cytoplasm of 50 percent of its affinity for methylene blue at pH 11.0. If a chorioretinopathy of presumable congenital origin is associated with cerebral calcification, the chances are approximately nine to one that serological tests will prove it due to congenital toxoplasmosis. If it is not associated with cerebral calcification, the chances are approximately nine to one that the chorioretinopathy is not due to toxoplasmosis. The use of sulfonamides is justified in pregnant women with high titer of antibody and no complement-fixing antibody to prevent toxoplasmic infection of the child. The use of sulfonamides is not of value in infants with congenital toxoplasmic retinopathies. Chas. A. Bahn.

19

CONGENITAL DEFORMITIES, HEREDITY

Burn, R. A. **Deafness and the Laurence-Moon-Biedl syndrome.** Brit. J. Ophth. 34:65-88, Feb., 1950.

The literature of the last ten years on Laurence-Moon-Biedl syndrome is reviewed in detail, and in addition all case reports mentioning deafness. Two new families with the syndrome are reported. From the detailed survey it is shown that the incidence of congenital deaf-mutism in these patients and their siblings is thirty times as high as in the general population. There is an excess of males which cannot be explained on the hypothesis of sex-linkage or any other theory. The relatives of the affected patients frequently are polydactous, but among the many anomalies accompanying the syndrome polydactyly is very rare. The mode of inheritance is best explained by assuming a single recessive autosomal mutant gene with multiple effects. The theory of two genes, one of them dominant, is tenable in some of the individual cases, but not in all. The hypotheses of sex-linkage, complete or partial, must likewise be rejected. This comprehensive report contains detailed summaries as well as full abstracts of the literature. (88 references.) Orwyn H. Ellis.

Halberg, G. P., and Paunessa, J. M. **An incomplete form of mandibulo-facial dysostosis (Franceschetti's syndrome).** Brit. J. Ophth. 33:709-713, Nov., 1949.

In 1944 Franceschetti and Zwahlen described a new syndrome of changes of the bony structure of the face and one or both eyes. A six-year-old boy presented a right amblyopia, right esotropia of 50°, left hyperphoria of 30°, abnormal retinal correspondence, obliquity of the palpebral fissures and irregularities of the eyelashes. In addition, his face showed superior prognathism, atrophy of the chin, atrophy of the malar bones and complete absence of the nasofrontal angle. The boy was mentally and otherwise physically normal. No treatment was offered.

Morris Kaplan.

Papolczy, F. **Bilateral congenital anopththalmos.** Brit. J. Ophth. 33:685-688, Nov., 1949.

A 6-months-old infant with bilateral anophthalmos, one of the rarest of developmental anomalies, is very briefly described. The infant was otherwise normal and well. Usually there is a family history of anophthalmos or other developmental anomalies. Morris Kaplan.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Currie, J. G. D. **Eye sight and industry.** Tr. Ophth. Soc. U. Kingdom 67:337-348, 1947.

The author advises the industrial ophthalmologist to visit the factories and investigate the type of work that is required, the lighting, and the position of the individual worker in regard to the light. Ventilation is also important; many cases of fatigue were due to improper ventilation or too great radiation of local heat. The ophthalmic surgeon should not certify men as fit to return to work when he does not know to what work the man is returning. Beulah Cushman.

Dansey-Browning, G. C. **Some wartime statistics.** Brit. J. Ophth. **33**:670-677, Nov., 1949.

The figures for ophthalmic injury or disease quoted in the Statistical Report on the Health of the Army, 1943-45, agree in the main with the expectations of military ophthalmologists. Morris Kaplan.

Peterson, A. D., and Noetling, F. **Preliminary report of progress of the eye program at R. R. Donnelley and Sons.** Tr. Am. Acad. Ophth. pp. 270-275, Jan.-Feb., 1950.

The results of a partial visual survey made in one of the largest printing plants in this country were so evident in increased efficiency that the management authorized a complete visual program for the entire company. Because of the importance of color discrimination in the printing industry, the Farnsworth-Munsell 100 hue color discrimination test was found most satisfactory. A report of the visual studies conducted with 336 employees, illustrating the degree of importance that vision has to performance on the job, is presented in detail.

Chas. A. Bahn.

Swanson, C. A. **Highlights of the Navy eye-correction, eye-protection program.** Tr. Am. Acad. Ophth. pp. 262-270, Jan.-Feb., 1950.

During the last war, the Navy supplied corrective and protective lenses for workers in hazardous eye occupations. Of 304,000 civilian employees 250,000 received the preliminary eye examinations and more than 18,000 were refracted. Sight screeners and Ortho-Raters were employed in the preliminary examinations. Refractions were preferably made by ophthalmologists at an average cost of $6.20 each. The results of the program in two groups of activities are described in some detail. In one, which involved 5,000 persons and several different trades, eye injuries were reduced from seven per million man hours to less than five. In the second activity, which included 1,300 workers, 15 eye injuries occurred during the first five months before the initiation of the program. Approximately one year after the installation of the program, no eye injuries occurred during two million man hours of work. Lost-time eye injuries averaged $60.00 each, including the cost of the medical care. The savings resulting from the program more than justified its cost. Chas. A. Bahn.

Esteban, Mario. **Visual requirements for automobile drivers.** Arch. Soc. oftal. hispano-am. **9**:1045-1066, Oct., 1949.

The visual requirements for chauffeurs in different countries are reviewed. In comparison with other countries the requirements in Spain are quite strict. The author proposes some changes, which if adopted would result in the following standards. For professional chauffeurs a total visual acuity (of the two eyes combined) of 13/10, with a refractive correction not exceeding plus or minus four diopters; a normal visual field; night vision after a 20 minute period of dark adaptation not less than 0.07 of day vision; adaptation time, after exposure to extreme light not exceeding three minutes; recognition of the red, yellow and green signals; stereoscopic vision of not less than 30 seconds; no paralysis of

the ocular muscles, and normal reactions to light and accommodation; no chronic conjunctivitis, epiphora, extensive symblepharon, chronic osteitis, and orbital neoplasms displacing the globe or interfering with its motility. For nonprofessional drivers a total visual acuity of 11/10, with a refractive correction not exceeding five diopters. With the exception of hemianopsia, the visual field may be restricted to 50 percent of normal but there must be no hemeralopia or diplopia and red, yellow, and green signal lights must be differentiated. Ray K. Daily.

Pires, A. A. **Industrial ophthalmology.** Rev. brasil oftal. **8**:175-190, March, 1950.

The author deals with the need for visual tests in industry, tests for color vision, the relationship of refraction to occupation, injuries by foreign bodies, protective glasses, protective helmets, work factors which may give rise to ocular disease, welding injuries, quantity of illumination, and evaluation of visual loss.
W. H. Crisp.

Soriano Fischer, Elisa. **Causes of blindness in Madrid.** Arch. Soc. oftal. hispano-am. **9**:1210-1219, Nov., 1949.

This is an analysis of the 4,386 applicants for blind aid. The data show that in 76.38 percent the blindness was preventable. 19.5 percent of the applicants were blind from infections, most of which were trachoma; 18.1 percent had cataracts of various types; 13 percent of blindness was due to myopia, with fundus lesions, and retinal detachment; 7.5 percent were blind through trauma; 6.1 percent from congenital lesions; 7.5 percent from leucomas; 9.1 percent from optic atrophy; 6.2 percent from uveitis, and 3.9 percent from glaucoma. The data indicate a need for an intensive campaign for prevention of blindness, and intensification of safety measures in industry. Patients with contagious ocular diseases should be isolated, treated, trained for work compatible with their visual acuity, and prevented from becoming a social menace. Young people with progressive ocular diseases should be educated for blindness, which is sure to overtake them in adult life. People with congenital and hereditary blindness should be instructed in the prevention of transmission of their lesion.
Ray K. Daily.

Vila Ortiz, J. M. **Industrial eye injuries.** Arch. Soc. oftal. hispano-am. **9**: 1161-1177, and 1304-1327, Nov. and Dec., 1949.

In this detailed discussion the factors which the author urges should be taken into consideration in fixing compensation are preexisting disease aggravated by the job, post-traumatic complications, negligence on the part of the worker or employer, penalty for malingering, evaluation of the visual disability on the basis of the job requirement, a differential in the percentage of disability depending on loss of vision, loss of the eyeball, and additional disfigurement. Compensation tables are presented for partial monocular and binocular disability, total monocular and bilateral blindness, partial monocular loss of vision in occupations requiring a high visual acuity, partial bilateral loss of vision in occupations not requiring fine visual acuity, partial loss of vision in monoculars, impairment of the visual fields, and disability due to sequelae other than visual loss. The establishment of a National Bureau on Ocular Disabilities is advocated to keep obligatory records of the ocular status at the time of employment and accident reports, and maintain a medical inspection service on the use of protective devices, which should be obligatory. Ray K. Daily.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

Deaths

Dr. Chester Tupper Cadwell, Passaic, New York, died January 23, 1950, aged 83 years.

Dr. Joseph William Charles, St. Louis, Missouri, died February 10, 1950, aged 81 years.

Dr. Theron Earle Fuller, Texarkana, Texas, died February 1, 1950, aged 65 years.

Dr. Joseph Wesley Kimberlin, St. Petersburg, Florida, died February 1, 1950, aged 76 years.

Announcements

Home Study courses

The 1950-1951 Home Study courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1st and continue for a period of 10 months. Registrations must be completed before August 15th. Detailed information and application forms may be obtained from Dr. William L. Benedict, executive secretary-treasurer, 100 First Avenue Building, Rochester, Minnesota.

Orthoptic examinations

Applications for the examination of orthoptic technicians to be conducted by the American Orthoptic Council in September and October, 1950, will be received by the office of the secretary, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., until July 1, 1950. Applications must be accompanied by the examination fee of $25.00.

Societies

New York alumni meeting

The first annual clinical meeting of the New York Eye and Ear Infirmary Alumni Association was held at the New York Eye and Ear Infirmary on May 11th and 12th. The program of the first day was devoted to otologic subjects.

Ophthalmic papers presented on May 12th were: "Recent advances in intracapsular cataract surgery," Dr. Elbyrne G. Gill (Discussion by Dr. Conrad Berens and Dr. Bernard Samuels); "Diagnosis and surgical treatment of fractures of the orbit causing enophthalmos and/or diplopia," Dr. Herbert Anthony (Discussion by Dr. Elbyrne Gill and Dr. Wendell L. Hughes); "Iridencleisis for glaucoma," Dr. John H. Sulzman (Discussion by Dr. Willis S. Knighton and Dr. Raymond E. Meek); "Removal of intraocular foreign bodies," Dr. A. Russell Sherman (Discussion by Dr. Truman L. Boyes, Dr. Loren P. Guy, and Dr. Byron Smith); "Lesions of the visual pathways with particular reference to the visual fields," Dr. Jay G. Linn (Discussion by Dr. Hunter Romaine and Dr. Robert McClanahan); "Casual observations in ocular therapeutics," Dr. William F. Ryan (Discussion by Dr. Daniel B. Kirby and Dr. Joseph Krug); "Present status of retrolental fibroplasia," Dr. Algernon B. Reese.

Carolinas to meet

There will be a joint three day meeting September 11, 12, and 13, 1950, of the North Carolina Society, Eye, Ear, Nose, and Throat, and the South Carolina Society of Ophthalmology and Otolaryngology. Headquarters will be the Skyland Hotel, Hendersonville, North Carolina.

The following otolaryngologists will be on the program: Dr. Fletcher D. Woodward, University of Virginia School of Medicine; Dr. Lester A. Brown, Emory University School of Medicine; Dr. B. T. Horton, Mayo Clinic; Dr. Donald F. Proctor, Johns Hopkins University School of Medicine.

Ophthalmologists to be present are: Dr. Bruce Fralick, University of Michigan School of Medicine; Dr. Edmund B. Spaeth, University of Pennsylvania School of Medicine; Dr. Frank B. Walsh, Johns Hopkins University School of Medicine; Dr. Richard G. Scobee, Washington University School of Medicine.

For further information please contact: Dr. MacLean B. Leath, secretary, North Carolina Society, Eye, Ear, Nose, and Throat, High Point, North Carolina, or Dr. Roderick Macdonald, secretary, South Carolina Society of Ophthalmology and Otolaryngology, Rock Hill, South Carolina.

CONDENSED CHAPTERS FROM

The History of the Guild

THE PHILADELPHIA GUILD

The cooperation that certain Philadelphia opticians had learned to practice during World War I, had tangible results after that when Pennsylvania enacted a law specifically licensing non-medical refraction.

The new law included a "grandfather's clause" under which any optician who had been examining eyes for a stated number of years, automatically qualified for a license.

The immediate result was a sharp division into two groups; opticians who chose to feature non-medical refraction, and those who elected to maintain their strictly dispensing type of operation.

The non-medical refractionists were aggressive. They got their story to the public in paid newspaper ads, in some instances including outright attacks on medical eye care, such as "warnings" against the "danger" of drops.

Obviously, here were charges that should be answered; but too big a job for any one individual. Here, then, was a specific need for cooperation among dispensing opticians; and a clear need, too, for an organization to handle the matter.

The result was the organizing of the Philadelphia Guild of Prescription Opticians which, interestingly enough, had as the specific purpose of its founding the objective of answering attacks against medical eye care.

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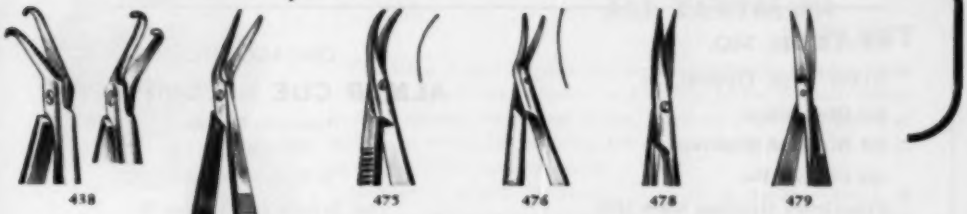

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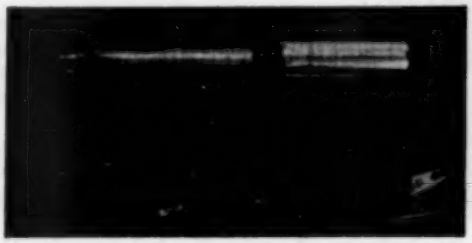

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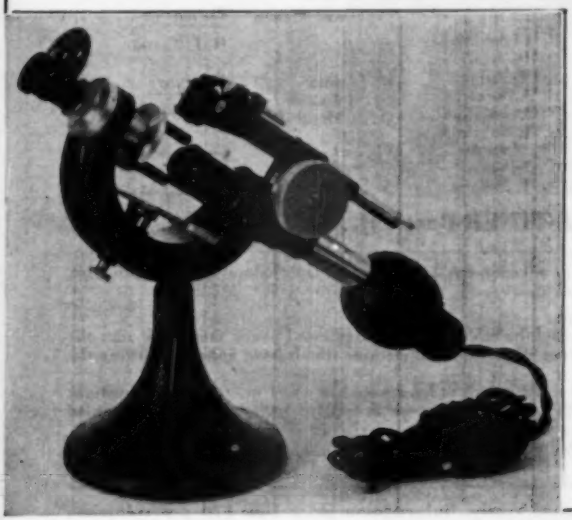

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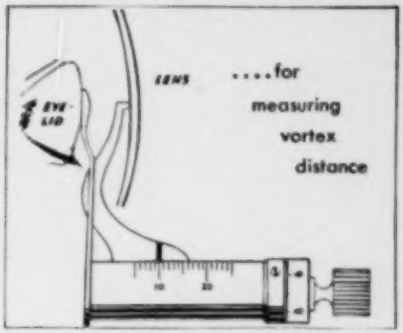

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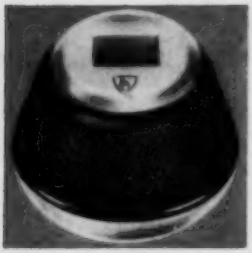

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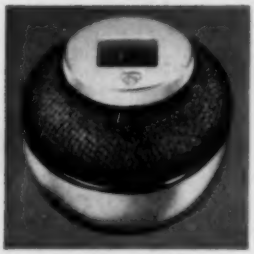

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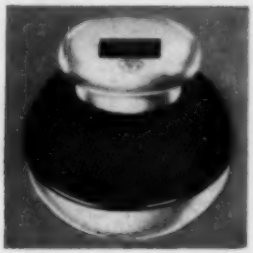

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